NON INVASIVE PREDICTOR OF OESOPHGEAL VARICES IN CIRRHOSIS- PLATELET COUNT/SPLEEN DIAMETER RATIO

Dissertation submitted to

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

In partial fulfilment of the regulations for

the award of the degree of

GENERAL MEDICINE

M.D. BRANCH – I

THANJAVUR MEDICAL COLLEGE,

THANJAVUR – 613 004.

THE TAMILNADU DR.MGR MEDICAL UNIVERSITY

CHENNAI – 600 032.

APRIL -2013

CERTIFICATE

This is to certify that this dissertation entitled "**NON INVASIVE PREDICTOR OF OESOPHAGEAL VARICES IN CIRRHOSIS-PLATELET COUNT/SPLEEN DIAMETER RATIO"** is a bonafide original work of **Dr.ASHWINI KAMATH** in partial fulfilment of the requirements for M.D Branch -I (General Medicine) Examination of the Tamilnadu Dr.M.G.R. Medical University to be held in APRIL - 2013. The period of study was from October 2011 to October - 2012.

Prof. DR.K.NAGARAJAN MD
UNIT CHIEF, M-3
DEPT. OF INTERNAL MEDICINE
THANJAVUR MEDICAL COLLEGE
THANJAVUR- 6130004

Prof. DR. S.MUTHUKUMARAN MD
HEAD OF THE DEPARTMENT
DEPT. OF INTERNAL MEDICINE
THANJAVUR MEDICAL COLLEGE
THANJAVUR- 613004

PROF.DR.C.GUNASEKARAN M.D.D.C.H,
DEAN I/C,
THANJAVUR MEDICAL COLLEGE,
THANJAVUR–613004

DECLARATION

I, **Dr. ASHWINI KAMATH**, solemnly declare that dissertation titled **"NON INVASIVE PREDICTOR OF OESOPHAGEAL VARICES IN CIRRHOSIS- PLATELET COUNT/ SPLEEN DIAMETER RATIO"** is a bonafide work done by me at Thanjavur Medical College, Thanjavur during October 2011 to October 2012 under the guidance and supervision of **Prof.Dr.K,NAGARAJAN. M.D.,** Unit Chief M-III, Department of Internal Medicine, Thanjavur Medical College, Thanjavur.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University towards partial fulfilment of requirement for the award of **M.D degree (Branch -I) in General Medicine**.

Place: Thanjavur
Date: **(Dr.ASHWINI KAMATH)**

ACKNOWLEDGEMENT

First and foremost I'd like express my gratitude to the God Almighty for everything.

I gratefully acknowledge and express my sincere thanks to **Prof. Dr.C.Gunasekaran M.D.D.C.H.,** Dean I/C, Thanjavur Medical College and hospital, Thanjavur for allowing me to do this dissertation and utilizing the Institutional facilities.

I am extremely grateful to **Prof Dr.S.Muthukumaran M.D.,** professor and Head, Department of Internal Medicine, Thanjavur Medical College and hospital, for his full-fledged support, valuable suggestions and guidance during my study and my post graduate period.

I am greatly indebted to **Prof Dr .K. Nagarajan M.D.,** my Professor and Unit Chief, who is my guide in this study, for his timely suggestions, constant encouragement and scholarly guidance in my study and Post Graduate period.

I express my gratitude to my respected Professors, **Prof Dr.P.G. Sankaranarayanan M.D, Prof Dr. S.Manoharan M.D, Prof Dr.C.Ganesan M.D., and Prof Dr.D.Nehru M.D, DMRD** for their Guidance and constructive criticism which enabled me to do this work effectively.

I would also like to extend my warmest gratitude to **Dr. C.Paranthagan** M.D, Registrar, Department of Internal medicine for his constant encouragement and support.

I express my gratitude to **Dr.J.Vijayababu M.D,D.M.**, **Dr. S.Vetrivel M.D and Dr.Thirumurugan.M.D**., Assistant professor of my unit for their valuable guidance and suggestions that made this work possible.

I would like to express my deepest gratitude to **Prof Dr. R.Ganesan M.D.D.M** and **Dr.C.Krishnan M.D.D.M**; Department of Medical Gastroenterology for their timely help and guidance throughout the study period.

I would like to express my sincere thanks to Prof Dr. **N.Sasivathanam M.D. DGO,** Head of Department of Biochemistry**,** for her sincere support in biochemical evaluation of patients.

I would also like to thank **J.S.Jesus Raja** for his excellent support in statistical analysis.

I would also like to thank all the medical and para-medical staffs who have helped me complete this study.

A special thanks to all the patients who willingly co-operated and participated in this study.

I would like to thank all my colleagues and friends who have been a constant source of encouragement to me.

Last but not the least; I would like to express my most sincere gratitude to my parents for their constant support and tolerance.

NONINVASIVE PREDICTOR OF OESOPHAGEAL VARICES IN CIRRHOSIS-PLATELET COUNT/SPLEEN DIAMETER RATIO

Ashwini kamath; S. Muthukumaran; K.Nagarajan; Department of Internal Medicine, Thanjavur medical college and hospital,Thanjavur

ABSTRACT:

BACKGROUND: Current guidelines recommend that all cirrhotic patients must undergo screening endoscopy for the presence of oesophageal varices. With increasing number of patients with chronic liver disease and their improved survival, these guidelines impose a burden on the endoscopic units, available facilities and also economically. In this study we aim to identify the value of Platelet count/Spleen diameter ratio as a non invasive predictor of oesophageal varices in patients with cirrhosis and its predictive efficacy.

MATERIALS AND METHODS: 60 patients with newly diagnosed cirrhosis admitted during a one year study period were evaluated prospectively. Patients with unstable vitals at admission, bleeders and history of prior treatment (medical or surgical) were excluded. All patients underwent biochemical work up, UGI scopy and ultrasonographic measurement for spleen diameter. Platelet count/spleen diameter ratio was calculated for all patients.

RESULTS: Platelet count/spleen diameter ratio was found to be significantly different in patients with oesophageal varices and in those without. At a cutoff of 909, it had a sensitivity of 95.2% and specificity of 88.8%. Prevalence adjusted positive predictive value of the test was found to be 95% and negative predictive value of 89%. It also correlated significantly with other non invasive parameters such as ascites, platelet count, splenomegaly and Child-Pugh score.

CONCLUSION: Platelet count/spleen diameter is valuable tool in non invasive prediction of oesophageal varices in patients with cirrhosis. Its use would avoid unnecessary endoscopy without a significant risk of missing oesophageal varices.

INTRODUCTION

Oesophageal varices are one of the most common complications of portal hypertension that accompanies liver cirrhosis. The prevalence of oesophageal varices may range from 60% to 80% in patients with cirrhosis, and the reported mortality from variceal bleeding is around 17% to 57%[1-4].

The Baveno III Consensus Conference on portal hypertension recommends that all patients with cirrhosis should undergo endoscopic evaluation for varices at the time of diagnosis[5]. To evaluate the progression of this feature, it has been proposed to repeat endoscopy in patients with no varices every 2-3 years and every 1-2 years in patients with small varices[6].

In a developing nation like ours where there is a relative lack of endoscopy units, the practicality of these guidelines is questionable. Moreover, they impose an additional burden on the available facilities and also economically.

In order to reduce this increasing burden many studies have attempted to identify non-invasive parameters to help predict the presence of any Oesophageal Varices. Parameters like spider angiomata[7], splenomegaly[8, 9], ascites[9, 10], prothrombin time/activity[7, 11](PT-INR), serum albumin[12], platelet

count[7-12], Platelet count/Spleen diameter Ratio[1, 13, 14] (PSR) have been shown as independent predictors for the presence of oesophageal varices. Hence this study was conducted to study the value of PSR as a non invasive predictor of oesophageal varices in patients with cirrhosis and its predictive efficacy.

AIMS AND OBJECTIVES OF THE STUDY

1. To identify Platelet Count/Spleen Diameter ratio as a non invasive index in predicting the presence of oesophageal varices in patients with cirrhosis.

2. To assess the Predictive value of Platelet Count/Spleen Diameter ratio in the non invasive diagnosis of oesophageal varices in cirrhotic patients.

REVIEW OF LITERATURE

CIRRHOSIS: EPIDEMIOLOGY AND DIAGNOSIS

End stage of chronic damage to the liver is cirrhosis, characterized by fibrosis resulting in destruction and distortion of normal liver architecture[15]. Functional liver tissue is destroyed and replaced by regenerating nodules that cannot cope with the normal liver functions. As the progressive cascade of liver tissue destruction continues relentlessly, the patient shows signs and symptoms of liver cell failure. Such a patient shows reduced physical, mental, biochemical functions, the final result of the process leading to complete liver cell failure and death.

CAUSES OF CIRRHOSIS:

Numerous infectious, chemical, autoimmune, hereditary and vascular factors have been implicated in the causation of chronic liver injury leading to cirrhosis.

Viral hepatitis

Hepatitis A infection is usually a nonfatal, self-limited disease where a short period of disability is followed by complete recovery. Acute liver

cell failure is of rare occurrence. Though when it does occur, it is usually sub massive necrosis without cirrhosis characterized by complete collapse of liver architecture.

Similar to hepatitis A, hepatitis E is a self-limited process. Though it does not contribute to cirrhosis, it may manifest as an acute fulminant hepatic failure in pregnant patients in their third trimester.

Unlike the other hepatotrophic viruses, Hepatitis B virus is a DNA virus. It may occur as an isolated entity or as a co infection with hepatitis D virus (delta infection) [15]. The presence of Hepatitis B infection is necessary for the infectivity of Hepatitis D, but the reverse is not true. Chronic hepatitis B infection may lead to cirrhosis and Hepatocellular carcinoma (HCC). There is an increased incidence of this infection in Asia and sub-Saharan Africa. The mortality rate is 16% for those with compensated disease and 65% to 86% for decompensated disease[16]. In untreated individuals with HBeAg positive chronic hepatitis B, the incidence of cirrhosis is from 2 to 5.4 per 100 person years with an estimated 5-year cumulative risk of 8% to 20% [17]. Predictors of progression to cirrhosis and mortality include persistent viral replication and older age. The presence of any other independent hepatotoxic factors like alcoholism, HCV co-infection may also contribute to progression to liver cell failure. In the EUROHEP cohort study, the cumulative incidence of hepatic

decompensation was 16% and the mean interval between the time of diagnosis of cirrhosis to the first episode of decompensation was 31 months[16, 17]. Survival dropped over 55% at 1 year and to 14% to 28% at 5 years following hepatic decompensation.

Hepatitis C virus may cause cirrhosis in 15% of patients and chronic infection in up to 80%[18]. The propensity to cirrhosis and HCC in hepatitis C infection is increased in patients who are also alcoholics.

While hepatitis A and B are vaccine-preventable infections, no vaccines are available for the prevention of hepatitis C, D or E infections

Alcohol

Alcohol is an important and common cause of liver disease and cirrhosis worldwide. Heavy alcohol intake may lead to cirrhosis in 1 to 2 years or may even manifest several years after cessation of the habit. Just as cigarette lung damage is measured in pack years, pint years can be used to measure alcohol damage, with 15 pint years being a reliable measure for cirrhosis (1 pt of whiskey per day for 15 years)[19].

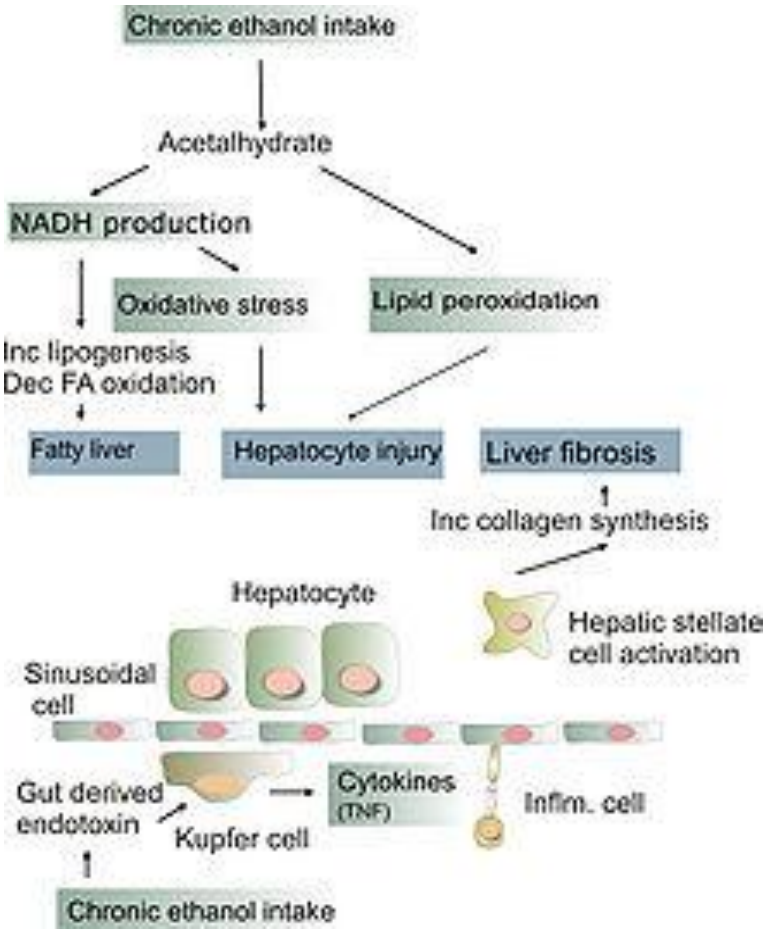
Identified risk factors:

- Quantity of alcohol: consumption of 60–80g per day (approximately 75–100 ml/day) for 20 years or more in men, or 20g/day

(approximately 25 ml/day) for women elevates the risk of liver disease by 7 to 47%[18]

- Drinking pattern: drinking outside of meal times increases the risk of ALDs by 2.7 times[20]
- Gender: females are more susceptible to alcohol mediated liver disease. Shorter duration and doses of chronic alcoholism is associated with development of ALD.[20]
- Hepatitis C infection: concomitant hepatitis C infection is known to significantly accelerate the cirrhotic process[20]
- Genetic factors: Monozygotic twins are more likely to be alcoholics and to develop liver cirrhosis than dizygotic twins. Polymorphisms in the enzymes involved in the alcohol metabolism, such as alcohol dehydrogenase (ADH), aldehyde dehydrogenase (ALDH), CYP4502E1, mitochondrial dysfunction, and cytokine polymorphism may play a role in genetic component. However, no specific polymorphisms have been currently firmly linked to ALD.
- Haemochromatosis(iron overload states)
- Diet: Alcoholics are usually malnourished due to lack of adequate nutritious diet and anorexia. This predisposes them to malnutrition, particularly vitamin A and E deficiency. This is significant as alcohol-induced liver damage may be aggravated by preventing regeneration of hepatocytes.[20]

Schematic representation of pathogenesis of alcohol mediated liver injury



Nonalcoholic fatty liver disease

There is an epidemic of obesity in adults and children in India and many other developed countries. Many of these may have nonalcoholic fatty liver disease (NAFLD) encompassing nonalcoholic steatohepatitis (NASH), which may progress to fibrosis and cirrhosis. Since this is an emerging entity, cirrhosis previously branded as 'cryptogenic' may actually have been secondary to NASH. The only valued treatment at present is weight reduction along with correction of lipid and glucose abnormalities. The changing trends of the modern era with its sedentary lifestyle and food faddism, the numbers of patients with obesity is on the rise. Thus more patients will progress to cirrhosis at an earlier age in the future.[21, 22]

Biliary cirrhosis

The pathological features of biliary cirrhosis differentiate it from post viral or alcoholic hepatitis, yet the manifestations of end stage liver disease are the same. Histopathological features are those of chronic cholestasis, xanthomatous transformation of hepatocytes, copper deposition and the irregular so-called biliary fibrosis.

Primary biliary cirrhosis (PBC), a disorder that often affects middle-aged women, is characterized by portal inflammation and necrosis of

cholangiocytes of small and medium sized bile ducts. Laboratory work up shows cholestatic liver enzyme abnormalities and positive antimitochondrial antibodies (AMA) [22].

On the other hand, Primary sclerosing cholangitis (PSC) typically affects young men. It is a chronic cholestatic condition occurring due to the diffuse inflammation and fibrosis of the entire biliary tree, the etiology of which remains unknown. Over 50% patients with PSC may have ulcerative colitis.[22] There is no specific serologic marker, perinuclear antineutrophil cytoplasmic antibody (pANCA) may be positive in up to 65%. The diagnosis is made by a "pruned tree" deformity of bile ducts on endoscopic retrograde cholangiopancreatography or magnetic resonance cholangiopancreatography.

Autoimmune causes

Autoimmune hepatitis, has unknown etiology and may cause progressive liver dysfunction.[23] The presence of antinuclear antibodies, anti-smooth muscle antibodies and increased serum gamma globulins aids in diagnosis. Typically these patients do not benefit from immunosuppressive medications such as steroids and azathioprine- wherein the disease is called 'burned out'. Other autoimmune disorders such as Sjögren syndrome, thyroiditis, glomerulonephritis, ulcerative colitis, celiac disease and juvenile

diabetes mellitus may be associated with an increased frequency in these patients.

Genetic disorders

The genetic diseases implicated in liver cirrhosis are α_1-antitrypsin deficiency, Wilson disease, and Hemochromatosis. Screening of all family members becomes mandatory when these disorders are diagnosed in any one among the family.

Cirrhotic patients with emphysema and children with cholestasis should be evaluated for α_1-antitrypsin deficiency.[24] Patients with ZZ phenotype are at greater risk of developing liver disease. Diagnosis is made by estimation of α_1-antitrypsin levels and phenotype. Liver biopsy shows characteristic periodic acid Schiff (PAS) positive, diastase resistant globules. Liver transplantation is the only effective and curative treatment available.

Wilson's disease is an autosomal recessive disorder and is characterized by mutation in ATP7B gene. Deficiency of this protein impairs biliary copper excretion thereby causing hepatic copper accumulation and oxidant damage secondary to copper toxicity. Young patients presenting with abnormal liver function tests, psychiatric and neurologic findings should be evaluated to exclude Wilson's.[25] Diagnosis

may be confirmed by 24-hour urine copper excretion, slit-lamp examination for Kayser-Fleischer rings and by liver copper quantification. Prompt treatment with zinc and/or trientine is advocated to prevent progression of disease.

Hereditary hemochromatosis characterized by hepatic iron accumulation is an inborn error of iron overload. It results in liver, cardiac, pancreatic, and joint dysfunction. Hepatic iron deposition leads to portal based fibrosis which may progress to cirrhosis and HCC. Iron studies in these patients reveal elevated transferrin saturation and high serum ferritin levels.[26] HFE mutation testing usually confirms the diagnosis. Therapeutic phlebotomy is the treatment of choice. Causes of secondary hemochromatosis are alcoholism, thalassemia major, multiple transfusions etc which may also progress to chronic liver disease.

Rare causes:

Infections: schistosomiasis, syphilis

Metabolic disorders: mucopolysaccharoidosis, glycogen storage disorders

Drugs: α-Methyldopa, Methotrexate, Amiodarone, Nitrofurantoin, Hypervitaminosis A

Miscellaneous: Sarcoidosis, Graft-versus-host disease, Budd-Chiari syndrome, chronic congestive heart failure (cardiac cirrhosis), chronic ductal obstruction (secondary biliary cirrhosis)

CLINICAL FEATURES:

The clinical picture of cirrhosis unfolds with progressive liver cell loss and dysfunction. It is characterized by the following features:

- Jaundice/Icterus - cutaneous and scleral yellowing due to inability of the liver to clear bilirubin.
- Spider angiomas/naevi- superficial spider-like cluster of capillaries composed of a central 'feeder' vessel and multiple minute tortuous and dilated radiating vessels with a peripheral erythema
- Bruising, subcutaneous ecchymosis, bleeding- decreased synthesis of clotting factors and low platelet counts.
- Muehrcke nails- nails with paired horizontal white bands
- Terry nails- nails with whitening of the proximal two thirds and reddening of the distal third.
- Digital clubbing.

- Dupuytren’s contracture- thickening of the palmar fascia, especially in alcoholics.

- Palmar erythema, gynecomastia, decreased body hair and testicular atrophy- due to elevated levels of estrogen in men. This contributes to decreased libido and infertility.

- Amenorrhea, breast atrophy and infertility in women

- Fetor hepaticus- a sweet odor in the breath of patients owing to decreased clearance of mercaptans.

- Parotid gland enlargement- painless swelling of the gland in the absence of obstruction of the Stensen’s duct.

- Asterixis- flapping tremors or liver flap, occur with increasing blood ammonia levels.

- Altered mentation and coma- decreased toxin clearance by the dysfunctional liver.

- Enlarged, tender liver may be palpated but more often, the organ is difficult to palpate because of fibrosis and shrunken state. This scarred organ causes resistance to blood flow and therefore, portal hypertension.

- Splenomegaly- due to portal hypertension and congestion.
- Varices (gastric and oesophageal) - Blood flow collateralizes into the gastric and esophageal venous system causing dilation of the veins.
- Hematemesis – rupture of the varices beyond a critical venous pressure. Major bleeds maybe life threatening.
- colonic varices and hemorrhoids- back pressure in portal system
- caput medusa- portosystemic collaterals around the umbilicus
- Ascites- increased shunting of pressure into the splanchnic circulation leads to shift of fluid into the abdomen, lower extremities, scrotum, or vulva. This is aggravated by hypoalbuminemia related to decrease hepatic protein synthesis. The risk of infection is also increased- spontaneous bacterial peritonitis (SBP). The presence of ascites is associated with a 50% survival at 2 years.

DIAGNOSIS:

The diagnosis of liver cirrhosis may remain elusive despite a thorough non invasive work up as there is no single biochemical or radiological parameter that correlates with specific liver injury or the extent of inflammation and damage. A combination of biochemical, radiological, clinical aids and histology are usually required. Invasive diagnosis through liver biopsy is the only definitive marker of progression to cirrhosis.

Biochemical Markers of Cirrhosis

As mentioned in the earlier text, there is no single biochemical marker of cirrhosis. A conventional liver function test (LFT) is usually initiated when signs and symptoms are present or when the stigmata of chronic liver disease are apparent. LFT comprises of alanine aminotransferase (ALT), aspartate aminotransferase (AST), fractionated bilirubin, alkaline phosphatase, prothrombin time (PT), and serum albumin estimation.

The AST, ALT, bilirubin, and alkaline phosphatase are not true indicators of hepatic function. AST and ALT are liver enzymes released into the circulation from damaged hepatocytes after hepatic injury. ALT is a cost-effective screening test for hepatic inflammation although it serves a

limited role in predicting the extent of inflammation and has no proven role in predicting the severity of fibrosis. [27]

The AST/ALT ratio is around 0.8 in normal subjects. In alcoholic hepatitis, the ratio is greater than 2:1.[28] In patients with NASH, the ratio is typically less than 1 and rises to greater than 1 with rising fibrosis score.[29] In these studies, AST/ALT ratio of more than 1 had a specificity of >75% and sensitivity of 32% to 83% for cirrhosis. [29] However, 2 additional studies failed to corroborate the predictive value of the AST/ALT ratio, and hence the clinical utility of this ratio remains unclear. [30]

The PT and serum albumin are accurate markers of hepatic synthetic function. A normal prothrombin time is maintained by the hepatic synthesis of clotting cascade proteins. With progression to fibrosis, the ability of the cirrhotic liver to synthesize these proteins diminishes leading to prolongation of PT. The PT helps predict survival in cirrhotics when used as a parameter in the Child-Pugh classification or model for end-stage liver disease (MELD) score. In a study by Croquet V., Vuillemin E., Ternisien C., et al, the PT consistently and accurately correlated with the degree of fibrosis of liver.[31] However, it is not specific marker for hepatic dysfunction. Disorders such as inherited coagulopathies, malabsorption syndromes and malnutrition can also account for abnormal clotting profiles.

Albumin which is also exclusively synthesized in the liver may also decrease with progression of liver disease. Similar to the PT, it is used in the Child-Pugh classification in determining the prognosis. Noncirrhotic conditions such as malnutrition, intestinal malabsorption and renal disease may also cause hypoalbuminenia. Low serum albumin also contributes to ascites and increases the risk of infections in cirrhosis.

Platelet count of less than 150,000 is defined as thrombocytopenia, which is a common finding in chronic liver disease. Platelet count of 50,000–75,000 may be found in approximately 13% of patients with cirrhosis.[32] Passive sequestration of platelets in the spleen has been implicated in the causation of thrombocytopenia in cirrhosis. However, recent research suggests impaired platelet production, increased destruction and functional disorders may also contribute to thrombocytopenia. Pilette C., Oberte F., Aube C., et al demonstrated the diagnostic accuracy of platelet count of< 1 60 000/l in prediction of large varices. It had a sensitivity of 80% and a specificity of 58%. Platelet count ≥260 000/L has a negative predictive value ≥91%.[7]

A multitude of combinations of biochemical markers have been proposed to increase the accuracy of diagnosing cirrhosis. These include the PT, gamma-glutamyl transpeptidase activity, FIB-4, Fibro test and serum apolipoprotein A1 concentration (PGA) index.

Progressive hepatic fibrosis is characterized by alteration in the extracellular matrix of the hepatic parenchyma[22]. Hence products of collagen synthesis, cytokines, chemokines and enzymes involved in fibrogenesis may be used as direct markers of liver fibrosis. Examples include procollagen peptide, laminin, matrix metalloproteinase, type IV collagen, transforming growth factor β, and hyaluronic acid. In spite of the remarkable progress made in direct, non invasive diagnosis of cirrhosis, their introduction has not eliminated the need for biopsy. Once the diagnosis of cirrhosis has been established, serologic and biochemical markers maybe be used for specific etiologic diagnosis (Table 1)[15].

Table 1 -- Biochemical and histological markers of causes of cirrhosis

Etiology	Biochemical Markers	Characteristic Histological Findings
ALD	AST/ALT >2 Elevated GGT	Mallory bodies Giant mitochondria Centrilobular fibrosis Ballooned hepatocytes
α_1-Antitrypsin deficiency	Decreased α_1-antitrypsin Pi type ZZ or SZ	Eosinophilic globules in periportal zones Periodic acid–Schiff deposits
Autoimmune hepatitis	Positive ANA titer Positive ASMA titer Positive LKM Ab	Lymphoid aggregates Prominent plasma cells Interface hepatitis

Etiology	Biochemical Markers	Characteristic Histological Findings
	Elevated globulins (especially serum IgG)	Rosetting of hepatocytes (Duct damage)
Hepatitis B	Positive HbsAg ± eAg positivity Positive HepB DNA Elevated ALT, AST	Ground glass cells containing HBsAg
Hepatitis C	Positive HCV Ab Positive HCV RNA Elevated ALT, AST	Bile duct damage Lymphocyte infiltration
Hereditary hemochromatosis	Fasting transferrin saturation >45% Elevated ferritin HFE gene mutation	Iron deposition within hepatocytes
Primary biliary cirrhosis	Positive AMA Elevated serum IgM	Loss of interlobular ducts Ductal inflammation “Florid duct” lesion Granulomas
Primary sclerosing cholangitis	Elevated p-ANCA	Bile duct scarring Concentric (“onion-skin”) fibrosis
Wilson disease	Ceruloplasmin <18 24-h urinary copper excretion >100 mcg	Copper deposits Focal, may be missed on biopsy Mallory bodies

Radiologic Findings in Cirrhosis[15]

No specific radiologic test can diagnose cirrhosis. Abdominal ultrasound, CT, and MRI are most useful in supporting the clinical or histological findings of cirrhosis. They identify manifestations such as hepatomegaly, hepatic nodularity, ascites, portal hypertension, portal vein thrombosis, portosystemic collaterals or varices and HCC.

Abdominal ultrasound is the most common and the first imaging modality used to evaluate cirrhosis. It is not only inexpensive but the results are easily reproducible and pose no risk of radiation or contrast exposure. A coarsened, heterogeneous echo pattern with surface nodularity on ultrasound characterizes a cirrhotic liver. Liver may appear atrophic in advanced disease. Caudate lobe hypertrophy is common. Sonographic ratio of caudate lobe width to right lobe width of 0.65 or more was demonstrated to have a sensitivity and specificity of 84% and 100%, respectively in diagnosis of cirrhosis as per a study by Harbin W., Robert N., Ferrucci J.[33]Portal hypertension is diagnosed by the presence of splenomegaly, ascites, and portosystemic collateral vessels on ultrasound. Doppler sonography can further identify thrombosis of portal and hepatic veins, dilatation of hepatic artery, portal vein and superior mesenteric vein. The reversal of normal portal

flow towards the liver, known as hepatofugal flow can be detected by color Doppler ultrasound.

Parenchymal distortion by cirrhotic process produces characteristic changes which can be easily recognized on contrast-enhanced CT and MRI. These changes are nodular liver margin, hypertrophy, atrophy of liver and fibrosis induced heterogeneity, steatosis, and iron deposition.

The radiologic changes become easier to identify as advanced disease sets in. Portal venous phase CT and magnetic resonance angiography can also detect portal vein thrombosis and flow, although these studies are expensive and provide no additional information over the convectional ultrasound with Doppler.

Histological Patterns of Cirrhosis

Liver biopsy is the gold standard in diagnosis of cirrhosis, the sensitivity and specificity ranging from 80% to 100%. Biopsy also aids in management and prognosis as it serves to grade and stage the severity of fibrosis. However, percutaneous transabdominal liver biopsy may result in perforated viscera, bleeding and infection.

Pathologic features that are common to all forms of cirrhosis include hepatic parenchymal necrosis, alteration in parenchymal architecture with nodular regeneration and scarring[22] Specific histological patterns seen in some types of cirrhosis are reviewed here.

Grossly, cirrhosis can be classified as micronodular, macronodular, or mixed.

In ALD the liver is grossly enlarged measuring 1500-2000g but with the advent of cirrhosis the liver shrinks. The liver surface is irregular and diffusely covered with small regenerative nodules that are less than 3 mm in diameter. This is described as micronodular cirrhosis [22] Mallory bodies and diffuse fat accumulation are seen on microscopy, but are not specific. The pericentral (centrilobular) [22] accumulation of fat can progress to complete obliteration of the central vein. When a thin band of connective tissue connects portal zones, the pattern is described as 'central-central' pattern. On Trichrome staining this gives a characteristic "chicken-wire" appearance. Electron microscopy shows collagenization of the space of Disse and Giant mitochondria.

Chronic viral hepatitis causes macronodular cirrhosis, characterized grossly by a dense, shrunken liver and large regenerative nodules connected by broad bands of connective tissue[22]. Microscopically,

irregular bands of connective tissue are prominent and involve three or more portal tracts in a single scar. In hepatitis B, HBsAg containing "ground glass hepatocyte" may be identified on hematoxylin and eosin stain. Bile duct damage and lymphocyte infiltration are prominent in cirrhosis caused by hepatitis C.

Cardiac cirrhosis is secondary to chronic congestive heart failure or constrictive pericarditis and resembles alcoholic cirrhosis. On gross inspection the liver is nodular and on microscopy centrilobular sclerosis can be identified[22] .The hallmark of cardiac cirrhosis is the presence of dilated, blood filled hepatic sinusoids[34].Breakdown of RBCs results in hemosiderin deposition and lipid laden macrophages. Fibrous bands bridge central areas with relative portal sparing. Cirrhosis caused by Budd-Chiari syndrome results from obstruction of the hepatic veins and can histologically be similar to cardiac cirrhosis with sinusoidal congestion and hepatic necrosis.

Biliary cirrhosis has typical histologic findings that include loss of interlobular bile ducts and ductal inflammation.[22, 34] Extensive portal tract damage results in a characteristic "jigsaw" (portal-portal) pattern of cirrhosis microscopically. Chronic inflammation around cholangioles and terminal plate disruption causes interface hepatitis which was previously

known as biliary piecemeal necrosis.[34] Copper deposition occurs, demonstrated with orcein stain. Central vein involvement is rare.

Distinguishing PBC on histology, an increased sinusoidal mononuclear infiltrate, portal-based granulomas and hepatocyte necrosis are observed. Ductal scarring and periductal fibrosis are classically seen in PSC[34]

The hallmark histological findings of other causes of cirrhosis are summarized in Table 1[15]

PROGRESSION TO DECOMPENSATED STATE

The natural history of cirrhosis is characterized by a prolonged asymptomatic compensated phase. The median survival from the time of diagnosis of compensated cirrhosis is 10 to 12 years. 60% of such patients progress to a decompensated phase in 10 years[35]. The likelihood of decompensation in individual patients is difficult to predict due to factors including the etiology of disease, amenability to treatment, hepatic reserve, other co-morbidities, the development of secondary infections and HCC. The ability to eliminate or treat the source of liver injury is of prime importance in delaying decompensation and prolonging survival. Alcohol abstinence has consistently demonstrated improved survival in alcoholic cirrhotics.[36] Interferon therapy in compensated HCV-related

cirrhosis and antiviral treatment for HBV-related cirrhosis retards the progression of cirrhosis and decreases the risk of development of HCC. [37]

The worsening of portal hypertension, hepatic insufficiency and the onset of complications heralds the transition from a compensated state to decompensation. These complications include jaundice, ascites, variceal hemorrhage, and encephalopathy[35,38]. Other complications like spontaneous bacterial peritonitis, hepatorenal syndrome, hepatic hydrothorax, portopulmonary hypertension, portal vein thrombosis and HCC may accelerate clinical deterioration. All these complications have a negative impact on the quality of life and prognosis. Cirrhotic patients should be vigilantly monitored for the development of these complications and targeted therapies should be undertaken to overcome these devastating clinical events. In many instances, the onset of hepatic decompensation serves as a clinical cue to initiate evaluation for liver transplantation in appropriate patients.

The rate of decompensation is 5% to 7% annually.[38]Median survival time plummets to approximately 2 years following decompensation. [35] The Baveno IV International Consensus Workshop[39] agreed upon a staging system based on natural history of the disease. The presence or absence of ascites, varices and variceal hemorrhage defines each of the

stages; the progression through which is accompanied by a dramatic increase in morbidity and mortality.

- Stage 1: the absence of varices and ascites. Probability of death at 1 year is 1%.
- Stage 2: The development of nonbleeding varices. Probability of death at 1 year is 3.4%.
- Stage 3: the onset of decompensated phase. Development of ascites irrespective of the presence or absence of nonbleeding varices. The 1-year mortality is 20%.
- Stage 4: the development of variceal bleeding with or without ascites.1-year mortality of 57%. Almost half of these deaths occur as a result of initial bleeding episode[38, 39].

Several prognostic models and scoring systems have been used to stratify disease severity and predict survival. The Child-Pugh score incorporating five variables (as depicted below) has been demonstrated to be a predictor of development complications and survival[40].

Factor	Units	1	2	3
Serum bilirubin	μmol/L	<34	34–51	>51
	mg/dL	<2.0	2.0–3.0	>3.0
Serum albumin	g/L	>35	30–35	<30
	g/dL	>3.5	3.0–3.5	<3.0
Prothrombin time	second prolonged	0–4	4–6	>6
	INR	<1.7	1.7–2.3	>2.3
Ascites		None	Easily controlled	Poorly controlled
Hepatic encephalopathy		None	Minimal	Advanced

Note: The Child-Pugh score is calculated by adding the scores of the five factors and can range from 5 to 15. Child-Pugh class is either A (a score of 5 to 6), B (7 to 9), or C (10 or above). Decompensation indicates cirrhosis with a Child-Pugh score of 7 or more (Class B). This level has been the accepted criterion for listing for liver transplantation.

The MELD score additionally uses serum creatinine and was initially designed to predict the mortality in patients undergoing transjugular intrahepatic portosystemic shunt placement.[41] It is now used to prioritize patients awaiting organ allocation and has proved to be a predictor of survival.

PORTAL HYPERTENSION:

Portal hypertension is defined as a portal pressure gradient exceeding 5 mm Hg[22]. It is a pathological process characterized by increase in portal venous pressure gradient between the inferior vena cava and portal vein.

ANATOMY, CAUSES AND HEMODYNAMIC PRINCIPLES:

The portal venous system drains the entire gastrointestinal tract except the proximal oesophagus and very distal rectum. It also drains the spleen, pancreas, and the gallbladder. Portal veins forms when the superior mesenteric vein and splenic vein coalesce behind the neck of the pancreas. The portal vein then traverses the gastrohepatic ligament to reach the hilum of the liver and divides into right and left portal veins. Then further branches out into portal venules which feed into the hepatic sinusoids. The sinusoids eventually drain into the hepatic veins, finally emptying into the retrohepatic inferior vena cava[42, 43].

Portal hypertension occurs from changes in portal resistance along with changes in portal blood flow, as defined by Ohm's law[43]:

$$\mathrm{P(pressure)} = \mathrm{Q(blood\ flow)} \times \mathrm{R(resistance)}$$

The mechanism of the rise in portal pressure depends on the cause and site of portal hypertension (table 2), cirrhosis being the most common cause[22]. In cirrhosis an increase in resistance to outflow of blood results in portal hypertension[22]. This results from a fixed component from disruption of hepatic architecture leading to the distortion of hepatic vascular pattern and a dynamic component from impaired intrahepatic vasodilatation. An intrahepatic decrease in the synthesis of the nitrous

oxide (vasodilator) [44], along with an increase in the production of the endothelin-1(vasoconstrictor) contributes to the dynamic component of increase in hepatic vascular resistance[45].

Table 2: Causes of portal hypertension[22,43]

Pre sinusoidal:

Prehepatic-

Portal vein thrombosis

Superior mesenteric vein thrombosis

splenic vein thrombosis or sinistral portal hypertension

Intrahepatic-

Primary sclerosing cholangitis

Primary biliary cirrhosis

Idiopathic portal hypertension

Sinusoidal:

Cirrhosis

Infiltrative disorders (e.g., myeloproliferative and lymphoproliferative diseases)

Vitamin A toxicity

Post-sinusoidal:

Budd-Chiari syndrome

Veno-occlusive disease

Congestive heart failure

Collaterals exist between the systemic venous system and the portal system. However owing to the lower resistance in the portal bed, blood flows from the systemic bed into the portal bed. With the development of portal hypertension there is a reversal of flow in these collaterals. In an attempt to decompress the ever increasing portal pressure, there is increase in size of the existing collaterals and development of newer ones due to angiogenesis. The locations and vessels involved in collateral formation are shown in table 3. Most patients have large collateral flow through the short and left gastric veins, hence forming gastro-oesophageal varices. Unfortunately these collaterals are insufficient to decompress the portal pressure and lead to complications including variceal bleeds and encephalopathy.

Table 3 -- Location and blood vessels of collaterals between the portal and systemic venous systems

Location	Portal System	Systemic System
Distal oesophagus and proximal stomach	Short gastric and left gastric (coronary) vein	Azygous vein
Rectum	Inferior mesenteric vein	Pudendal vein
Umbilicus (caput medusa)	Left portal vein	Umbilical vein
Retro peritoneum	Mesenteric veins	Renal vein or iliac veins

Portal pressure is measured by the hepatic vein pressure gradient (HVPG). It is the difference between the wedged hepatic venous pressure (reflecting the sinusoidal pressure) and free hepatic vein pressure[46]. Measurement of the HVPG in combination with pressure measurements of right heart, venography and transjugular liver biopsy delineates the site i.e., sinusoidal, presinusoidal or postsinusoidal.

Varices form when HVPG is more than 10 mm Hg and they tend to bleed when it exceeds 12 mm Hg [47]. But this is not applicable in all patients. Certain local factors are also involved in increasing the variceal wall tension[48]. Frank's modification of Laplace's law defines the wall tension as: T = (P varices – P esophageal lumen) × (radius of varix)/wall thickness. The varix ruptures when the variceal wall thins out and the tolerated wall tension is exceeded, the varix increases in pressure and diameter. Large varices at sites of limited soft tissue support especially at the gastroesophageal junction are at greater risk of rupture and bleeding.

OESOPHAGEAL VARICES: DIAGNOSIS AND CURRENT STAGING

The gastroesophageal area is the main site of varix formation[49]. The gastric portions of the varices extend for 2 to 3 cm into the fundus. Along the lesser curvature, they drain into the left gastric or coronary vein and into the portal vein. Along the greater curvature, they drain through the short gastric veins into the splenic vein. Dilation of these veins causes gastric varices. The collaterals in the submucosa do not communicate with the periesophageal veins in the lower 2-3 cms of the oesophagus and hence cannot be easily decompressed. Above this level, the varices can extend upwards but easily decompress through the perforating veins. This is why oesophageal varices bleed only at the lower end, and is the site where various therapies should be targeted.

All patients diagnosed with cirrhosis must be screened for Oesophageal Varices. It should be suspected in patients with spider nevi, jaundice, caput medusa, splenomegaly, ascites and encephalopathy.

DIAGNOSIS OF OESOPHAGEAL VARICES

1. UPPER GASTRO-INTESTINAL SCOPY (UGI SCOPY):

It is the most common method employed and current guidelines recommend that all cirrhotic patients should undergo UGI SCOPY to

screen for varices. If no varices are found, a repeat UGI SCOPY should be performed in 2 to 3 years and if small varices are seen, UGI SCOPY should be repeated in 1 to 2 years or at onset of decompensation, whichever is earlier[6].

As it enables direct visualization of the varices, it is the gold standard for diagnosis of oesophageal varices and helps in decision making by assessing the size and the presence of cherry spots and red wale signs. Also, it allows for prophylactic or therapeutic variceal band ligation in the same sitting.

Techniques adapted in diagnosis of varices on UGI SCOPY-

i. Examination for varices should be performed during withdrawal of the scope.
ii. The oesophagus must be maximally inflated, thus flattening out any folds masquerading as varices.
iii. Varices must be described as to their location in the oesophagus (lower, middle, or upper) and their size (small [<5 mm, Fig. 2] or large [>5 mm, Fig. 3]).
iv. Lower oesophageal varices are at maximum risk of bleeding and therefore should be graded and described.

2. CAPSULE ENDOSCOPY:

Capsule endoscopy (CE) uses the Pill Cam Eso measuring 26 by 11 mm. Initial pilot studies demonstrated that this device is well tolerated and safe[50]. A meta-analysis by Lu and colleagues[51] showed a pooled sensitivity and specificity of 85.8% and 80.5% respectively for detection of oesophageal varices. Many studies have shown good patient tolerance and satisfaction with CE as compared to UGI SCOPY[52]. With lower sensitivity and specificity than UGI SCOPY, it is a less effective mode of diagnosis, but may be considered in patients unable to tolerate UGI SCOPY or unwilling to undergo the procedure.

3. ENDOSONOGRAPHY:

Endoscopic ultrasound (EUS) examination of the portal vasculature is not routinely used for screening for oesophageal varices. EUS is as good as UGI SCOPY in identifying clinically significant oesophageal varices but better than UGI SCOPY in identifying gastric varices[53]. The EUS has been also used to study predictors for recurrence of varices after therapy. The presence and size of para-oesophageal varices were associated with recurrent varices. EUS can also be used to predict the risk of bleeding by estimating the variceal wall tension when combined with endoscopic manometry and to guide therapy.

4. ULTRASONOGRAPHY(USG):

Ultrasound examination is the most commonly employed technique in evaluation of cirrhosis. In combination with Doppler it can identify complications of portal hypertension such as ascites and development of collaterals. Findings such as splenomegaly, portosystemic collateral blood flow and reversal of flow in the portal vein are indicative of portal hypertension. The portal vein diameter has been studied as a screening parameter for detection of oesophageal varices, wherein a portal vein diameter of more than 13 mm correlates with the presence of varices (odds ratio 2.92 [95% CI 1.2–6.4])[11, 54]. It can also demonstrate thrombosis in the portal or splenic vein.

5. **TRANSIENT ELASTOGRAPHY** (TE)

It measures liver stiffness by employing pulse echo ultrasound readings. Since advanced fibrosis and cirrhosis leads to portal hypertension, an association with the degree of liver stiffness on TE with the presence of oesophageal varices has been studied. Kazemi F and colleagues[55] found that liver stiffness of less than 19 kPa had a negative predictive value of 93% for small oesophageal varices. In patients resistant to any invasive procedures, TE appears to be a good screening tool.

6. COMPUTER TOMOGRAPHY (CT):

CT can identify the cirrhotic configuration of the liver and signs of portal hypertension such as ascites, splenomegaly and collateral vessels. (Fig. 6). Helical liver CT had variceal detection rates of 92% for large varices and 53% for small varices as compared to UGI SCOPY.[56]Multidetector CT scans of the abdomen had a sensitivity and specificity of 90% and 50% respectively for diagnosing large oesophageal varices[57]. CT also identified a significant number of other pathologies like gastric, perioesophageal varices and extra luminal pathologies. Patients also showed better compliance with CT.

7. MRI

MRI with elastography is being studied to determine fibrosis in the liver. MRI also provides an excellent view of the vascularity of the liver and the flow through the portal and azygous veins. Flow in the azygous veins were higher in subjects with portal hypertension than in normal controls and peaked at midnight which helps guide the timing of treatment with beta blockers[58]

Gadolinium-enhanced MRI had a sensitivity of 81% in detecting oesophageal varices[59]. A significant correlation was seen in the grading of varices between endoscopy and MRI.

GRADING OF OESOPHAGEAL VARICES:

Endoscopic grading of oesophageal varices is subjective and there is considerable interobserver variability. Three grading systems are well known: by Dagradi[60] (1972); by the Japanese Research Society for Portal Hypertension (JRSPH, 1980)[61]; and by the North Italian Endoscopy Club for the Study and Treatment of oesophageal varices (NIEC, 1988).[62]

- Dagradi classifies oesophageal varices into five grades:

I: 1 to 2 mm in diameter, and straight or sigmoid shaped.

II: Similar to stage I but visible without occluding blood flow in the vessel.

III: 3 to 4 mm in diameter and straight or tortuous.

IV: 4 to 5 mm in diameter, tortuous, often coiled, seen in all quadrants of the oesophagus.

V: Greater than 5 mm in diameter, tightly packed, grape-like, covered by thin, wrinkled mucosa, with overlying cherry red spots and telangiectasias.

- The JRSPH system grades varices based on location, form, color, and red color sign:
    - The location of varices may be upper, middle, or lower third of the oesophagus.
    - The form is classified as small and straight (F1), enlarged and tortuous (F2), or large and coil shaped (F3).
    - The color of the varices is graded as white (Cw) or blue (Cb).
    - Also included is the presence of the red color sign (RC) that are dilated, small vessels (red wale sign), and telangiectasias or cherry-red spots on the surface of the varices (Fig. 8).
- The NIEC index takes into account the following
    - The Child-Pugh class of cirrhosis (A, B, or C)
    - Variceal size (small, medium, or large)
    - Presence of red color signs (absent, mild, moderate, or severe).

Of these, oesophageal varices size and red color signs are the most important signs. When compared with each other in a study by Rigo G.P and colleagues[63],the JRSPH and NIEC classifications were found to have high specificity in predicting variceal bleeding (93.4% and 94.8%, respectively) but not sensitive. All the three systems had low positive predictive values. None the less, the NIEC and JRSPH classifications are commonly used to describe oesophageal varices in investigative and clinical settings.

The **Baveno** I consensus conference recommends that oesophageal varices should be classified as small (<5 mm) and large (>5 mm) [64]. This cutoff of 5 mm was confirmed as being optimal to differentiate small from large varices. The guideline for primary prophylaxis of oesophageal varices differs based on whether varices are small or large. Patients with large-size varices, red color signs and Child-Pugh class C have the highest risk for bleeding within 1 year.

PROPHYLACTIC TREATMENT OF OESOPHAGEAL VARICES:

1. Pharmacologic modalities

Nonselective beta-blocking drugs such as propranolol and nadalol are the first line modality for primary prophylaxis. They inhibit the beta-

adrenergic receptors mediated vasodilatation, allowing unopposed alpha-adrenergic receptor mediated vasoconstriction in the mesenteric arterioles. This effectively reduces portal venous inflow and hence the pressure. They also reduce cardiac output hence further decreasing the portal inflow. Meta-analysis of various clinical trials shows that the beta-blocker therapy decreases the risk of bleeding oesophageal varices by 25% to 15% when compared with placebo[65]. The HVPG accurately assess the effectiveness of this therapy. A sustained decrease in the HPVG < 12 mm Hg is the best predictor of successful treatment[47] though this approach is not routinely and widely applied to clinical practice. Clinically the efficacy of beta blockers is monitored by a reduction in the resting heart rate of more than 25%. Only 20% to 30% of patients achieve these endpoints while 15% to 20% do not tolerate these doses, which may require discontinuation.

Nitroglycerin (short acting) or Isosorbide mononitrates(long-acting) are nitrates which cause venodilatation. This causes a decrease in portal venous blood flow and decreases the portal pressure. They do not affect the intrahepatic resistance. As they failed to demonstrate consistent results in various clinical trials, nitrates are not recommended for primary prophylaxis anymore.

Endothelin receptor antagonist and liver-selective nitrous oxide donors that specifically target intrahepatic vascular resistance are promising future investigational therapies[66].

2. Endoscopic sclerotherapy

Prophylactic endoscopic sclerotherapy (EST) initially was found to significantly reduce the risk of variceal bleed and improve survival. But subsequent trials failed to demonstrate this survival benefit. EST may actually provoke bleeding that may be difficult to control and may further increase mortality[67]. Consequently, EST is not recommended for prophylaxis of oesophageal varices[43].

3. **Endoscopic variceal ligation**

Endoscopic variceal ligation (EVL) significantly decreases the risk of first bleeding episode when compared with propranolol [68], with a relative risk reduction of 40%.Though no survival benefit over propronolol was demonstrated. It is also known to be associated with fewer complications than EST.

In summary, EVL and non selective beta blockers are recommended first-line modalities for primary prophylaxis of variceal hemorrhage. In patients who do not tolerate beta blockers EVL may be used.

MANAGEMENT OF AN ACUTE OESOPHAGEAL VARICES BLEED:

The management of an acute oesophageal varices bleeding includes hemodynamic resuscitation, achievement of hemostasis, prevention of complications and supportive treatments. The systolic blood pressure should be maintained at least at 90 to 100 mm Hg and a hemoglobin level around 9 g/dL (hematocrit of 25–30). A rebound increase in portal pressure has been identified with overzealous transfusion and which may precipitate early rebleeding [69]. Correction of coagulopathy is by using platelets (platelet count <50,000/ml) and Fresh frozen plasma. However they can also induce volume overload and lead to rebound portal hypertension. Recombinant factor VII use has shown to improve hemostasis, but no survival benefit was demonstrated[70].

Infections are associated with an elevated risk of rebleeding episodes and higher mortality[71]. Spontaneous bacterial peritonitis, pneumonia and urinary tract infections are commonly encountered. A complete microbiological work-up should be performed. Many clinical trials have demonstrated an improvement in bleeding control and patient outcomes with empirical institution of therapy with third generation

cephalosporins[72]. Therefore this antibiotic therapy should be initiated without delay.

PHARMACOLOGIC THERAPY:

Vasopressin and its analogs

Vasopressin is an endogenous nonapeptide that causes vasoconstriction in the splanchnic bed through its action on V1 receptors of the arterial smooth muscle. This reduces the portal venous inflow and hence the portal pressure. Its toxic effects include bowel necrosis from severe vasoconstriction. A semi synthetic analog, Terlipressin, has a lower incidence of systemic toxicity. It increases survival in subjects who have variceal bleeding[73].

Somatostatin and its analogs:

Somatostatin has a half-life of 1 to 3 minutes in circulation. It inhibits the release of glucagon, thereby decreasing portal pressure and collateral blood flow[74].

Octreotide has a longer half-life of 80 to 120 minutes. Although its effects on decreasing portal pressure is not prolonged. Early institution of vapreotide may be associated with better bleeding control but without a significant decrease in mortality[75].

ENDOSCOPIC TREATMENTS:

Endoscopic sclerotherapy

EST involves the injection of a sclerosant into or adjacent to a varix. This technique has been supplanted by EVL. Complications of the procedure include ulcers and ulcer-related bleeding, perforation and strictures. Current data does not support emergency EST as first-line treatment in acute bleeding oesophageal varices[76].

Endoscopic variceal ligation

EVL is the preferred modality for arrest of acute oesophageal varices bleed and for preventing rebleeds[22]. Varices at the GE junction are banded first, and then more proximal ones are banded in a spiral manner at 2 cm intervals. Varices in the middle or proximal oesophagus are associated with lower risk of bleeding and need not be banded. It requires fewer sessions to achieve obliteration of varices.

In summary, in control of active esophageal variceal hemorrhage the first line treatment includes a combination of pharmacologic intervention (i.e., octerotide) and EVL. 80% to 90% of patients achieve good hemostasis with first-line therapy; the remaining either fail to achieve hemostasis or have early rebleeding[77].

Bleeding that occurs more than 48 hours after the initial admission for hemorrhage and is separated by at least a 24-hour bleed-free interval is considered as rebleeding[43]. Factors associated with failure to control active bleeding and early rebleeding are summarized in table 4.

Table 4: Risk factors for re-bleeding or continued bleeding[43]

Failure to control acute hemorrhage
Spurting varices, infection ,high HVPG, high Child-Pugh score, Portal vein thrombosis
Factors associated with early rebleeding
Severe initial bleeding, infection, over enthusiastic volume resuscitation High HVPG, renal failure, Complications of endoscopic therapy
Factors associated with late rebleeding
High Child-Pugh score, continued alcohol use, Large varices, Hepatocellular carcinoma

In patients with uncontrolled active bleeding, definitive salvage therapy should be initiated at the earliest. Balloon tamponade produces effective hemostasis in 80% to 90% cases[78]. Airway should be secured to prevent aspiration. It is associated with a high risk of rebleeding on

deflation of the balloon and with pressure necrosis if kept inflated for > 48 hours. Therefore it is used as a bridging treatment until definitive treatment can be started.

EVL can be attempted a second time for early rebleeding. The salvage treatment in such patients is portal decompression surgeries, with transjugular intrahepatic portosystemic shunts (TIPS) being the procedure of choice.

Transjugular intrahepatic portosystemic shunts (TIPS)

TIPS decreases the elevated portal pressure by creating a communication between the hepatic vein and an intrahepatic branch of the portal vein. It produces effective hemostasis in over 90% patients[79]. The prognosis becomes dismal with the occurrence of complications from bleeding such as aspiration pneumonia or multiorgan failure. Patients with aspiration pneumonia have been demonstrated to have a 10% survival at 30 days[80]. The MELD score (discussed earlier) is the best predictor of mortality following TIPS.

Contraindications to TIPS are portal vein thrombosis with cavernoma formation, severe hepatic failure, severe congestive cardiac failure, severe pulmonary hypertension and polycystic liver disease. Surgical decompression using portosystemic shunts is also a salvage

modality, but its use has declined due to the increasing availability of TIPS and a higher associated morbidity.

Secondary prophylaxis

Following an index bleed, 70% patients have a recurrent variceal hemorrhage within 1 year[81], and have 70% 1-year mortality. The risk of rebleeding is highest in the first 6 weeks, with over 50% of these occurring within 3 to 4 days. Risk factors include severe initial bleed, Age >60 years, large oesophageal varices, severe liver disease, renal failure, continued alcohol intake and the presence of a hepatoma[82].

The first-line therapy for secondary prophylaxis of oesophageal varices hemorrhage is EVL and beta-blockers. A meta-analysis demonstrated that TIPS is superior to endoscopic treatment in the prevention of rebleeding (19% versus 47%)[83], but this advantage is offset by its higher morbidity owing to the development of hepatic failure and encephalopathy (34% versus 19%), failure to prolong survival and its lack of a cost benefit[84]. Hence TIPS is used as a salvage therapy in patients with recurrent hemorrhage despite adequate primary treatment.

In summary, modalities recommended for secondary prophylaxis of oesophageal varices hemorrhage are as follows[43]:

1. Eradication of oesophageal varices by EVL (every 1-2 weeks until varices are obliterated) with concomitant use of nonselective beta-blockers (propranolol or nadolol)

2. Nonselective beta-blocker therapy can be used alone if EVL is unavailable or contraindicated

3. TIPS is considered if endoscopic and pharmacologic therapies fail. (Recurrence of bleeding despite at least two sessions of endoscopic treatment done not more than 2 weeks apart).

Prevention of recurrent hemorrhage, preservation of liver function, maintenance of renal function, prevention of ascites and abstinence from alcohol are known to prolong survival. Orthotopic liver transplant is the only modality of treatment that is able to achieve most of these objectives and hence prolongs long-term survival. Always consider liver transplantation if the patient is Child-Pugh B or C.

METHODOLOGY

STUDY DESIGN

This is a non randomized, single center prospective study which analyses the correlation between clinical features, biochemical data and ultrasonographic findings with the presence of oesophageal varices in patients with cirrhosis. The study aims at identifying PSR as a non invasive tool in diagnosis of oesophageal varices in patients with advanced liver disease and to assess its predictive value.

STUDY CENTRE

This study was carried out at The Department Of Internal Medicine and The Department of Medical Gastroenterology , Thanjavur Medical College Hospital , Thanjavur, Tamil Nadu, India. All the patients admitted during the study period with features of cirrhosis and portal hypertension that was newly diagnosed underwent clinical examination, blood tests, ultrasound abdomen and UGI endoscopy. The findings were recorded in the proforma annexed herein. The data hence obtained was recorded in the master chart annexed herein.

STUDY PERIOD

Newly diagnosed cases of cirrhosis with portal hypertension admitted during the period October 2011 to October 2012 were included in this study. A total number of 60 cases, 41 males and 19 females were studied.

INCLUSION CRITERION:

1. Patients newly diagnosed of cirrhosis and portal hypertension, admitted between October 2011 and October 2012.
2. Patients over the age of 13 yrs.
3. H/o atleast 6 months of abstinence from alcohol

EXCLUSION CRITERION:

1. Patients with unstable vitals at admission.
2. Active gastrointestinal bleeding at admission(bleeders)
3. H/0 treatment for oesophageal varices- band ligation, sclerosis
4. H/o Transjugular intrahepatic portosystemic shunt (TIPS), or any surgery for portal hypertension.
5. H/o taking drugs for primary prophylaxis of variceal bleeding.
6. H/0 active alcohol abuse

STUDY CHARACTERISTICS:

Age, gender and the etiological diagnosis were recorded for all the patients. All patients were subjected to biochemical analysis including liver function tests, serum albumin estimation, PT-INR (prothrombin time-international normalized ratio). Platelet counts were checked using cell counters and then by manual method. All patients underwent abdominal ultrasonographic examination for measurement of diameter of spleen (in mms). Spleen diameter was determined based on the longest dimension of spleen on ultrasound.

Ultrasonographic findings were recorded by an experienced sonologist.

All the patients underwent UGI endoscopy to determine the presence and size of oesophageal varices. The criteria proposed at the Baveno I Consensus Conference were used to further classify the varices into small and large. Varices that flatten with insufflations of saline or minimally protrude into the oesophageal lumen were deemed small varices and those with presence of confluence (varices protruding into the lumen and touch each other), or that obscure at least 50% of the oesophageal lumen was called large varices. All the endoscopies were carried out by an experienced gastroenterologist in a single endoscopy unit.

The PSR was calculated for all the patient using the serum Platelet Count (in N/mm3) and Spleen Diameter (in millimeters).

All the patients were further stratified according to Child - Pugh's criteria under classes A, B and C. The data hence obtained were all recorded in the master chart annexed herein.

RESULTS AND OBSERVATION

FREQUENCY TABLES

In this study, all patients with newly diagnosed cirrhosis were stratified into three age groups as depicted below. The highest number of patients was between the ages 26- 50 years, which comprised of 66.7% of the study population. This was followed by 21.7% of patients over 51 yrs and 11.7% below 25yrs

TABLE 5: AGE DISTRIBUTION

Sl.no	Particulars	No. of respondents (n=60)	Percentage (100%)
1	Below 25yrs	7	11.7
2	26 to 50yrs	40	66.7
3	51yrs & above	13	21.7

CHART 1:

PIE CHART SHOWING AGE DISTRIBUTION

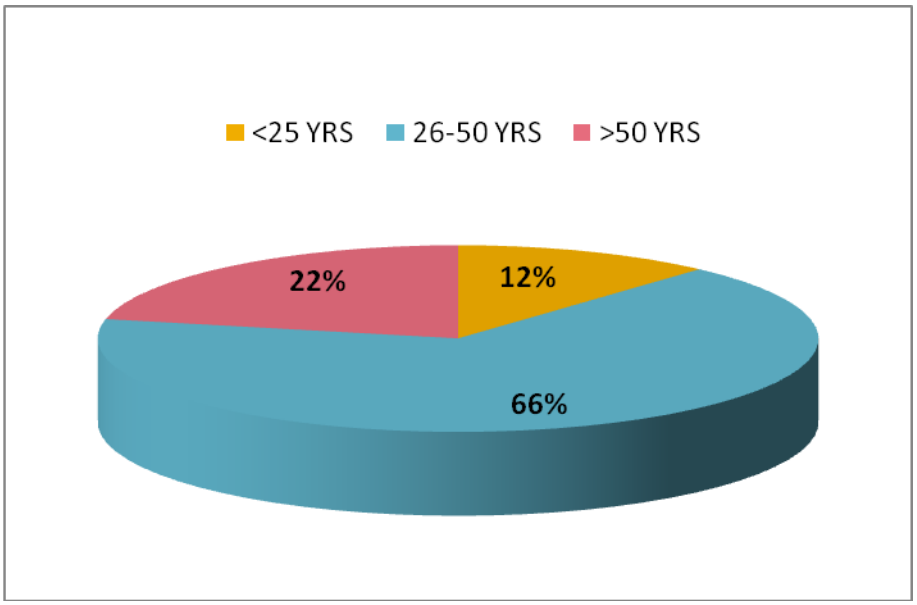


TABLE 6: GENDER DISTRIBUTION

Sl.no	Particulars	No. of respondents (n=60)	Percentage (100%)
1	Male	41	68.3
2	Female	19	31.7

Out of 60 patients included in the study group, 41 were male and 19 were female. Male to female ratio was 2.1:1. This shows a clear male preponderance.

CHART 2:

PIE CHART SHOWING GENDER DISTRIBUTION

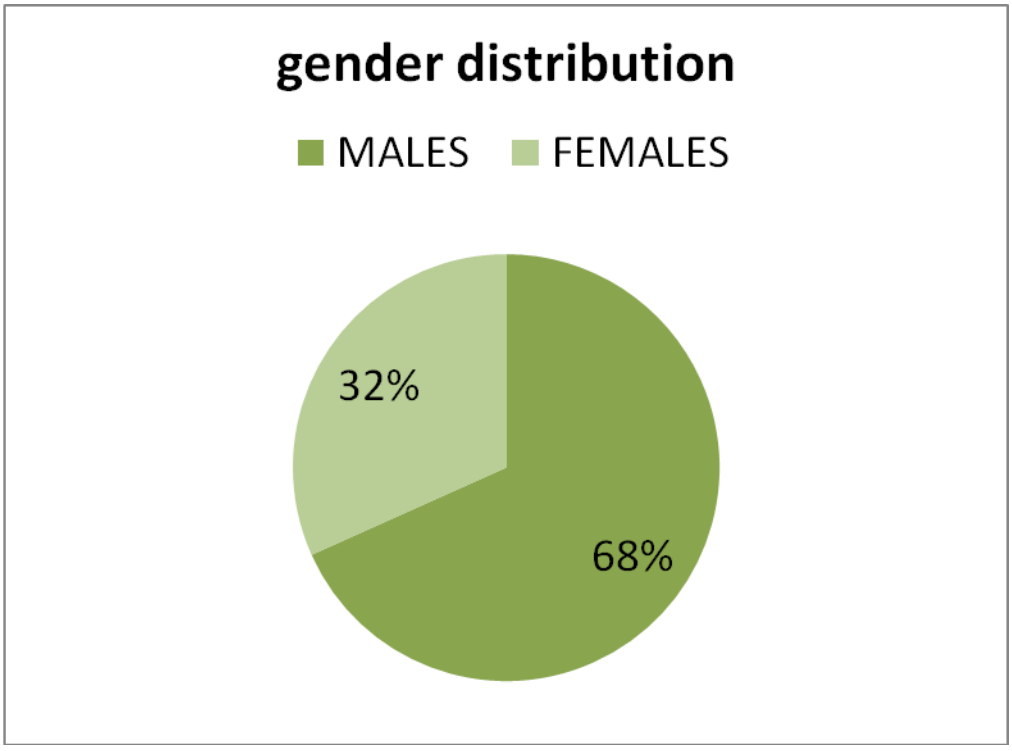
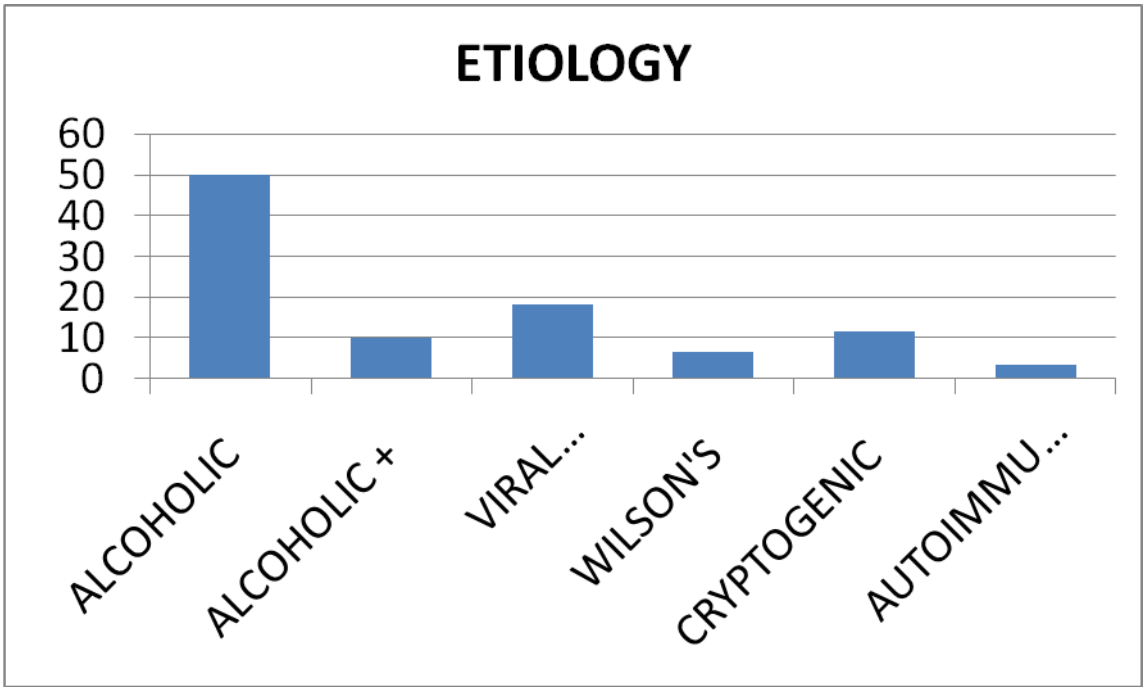


CHART 3: ETIOLOGY

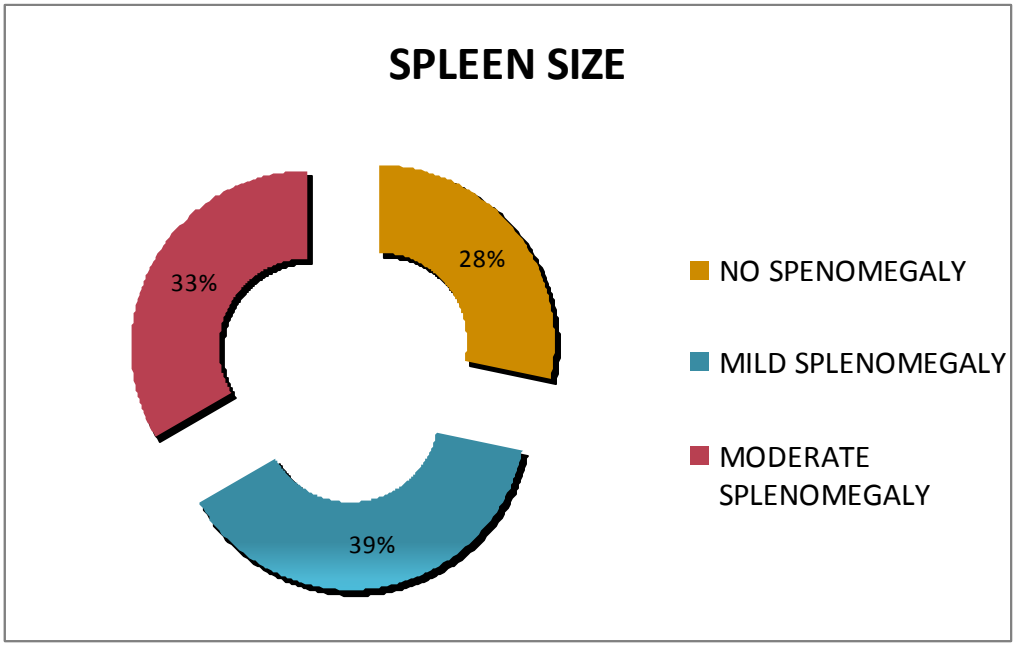


As depicted in the above chart, alcoholism was found be the most common etiology of cirrhosis (50%) in this study population, followed by viral hepatitis (hepatitis B and hepatitis C) and cryptogenic cirrhosis. Other causes of cirrhosis accounted for less than 10% cases.

SPLEENOMEGALY:

On clinical examination, splenomegaly was recorded as absent, mild and moderate spleen. Massive splenomegaly was not seen in this study hence excluded. No spleen enlargement was found in 17 patients (28.3%), mild splenomegaly in 23 patients (38.3%) and moderate splenomegaly in 20 patients (33.3%).

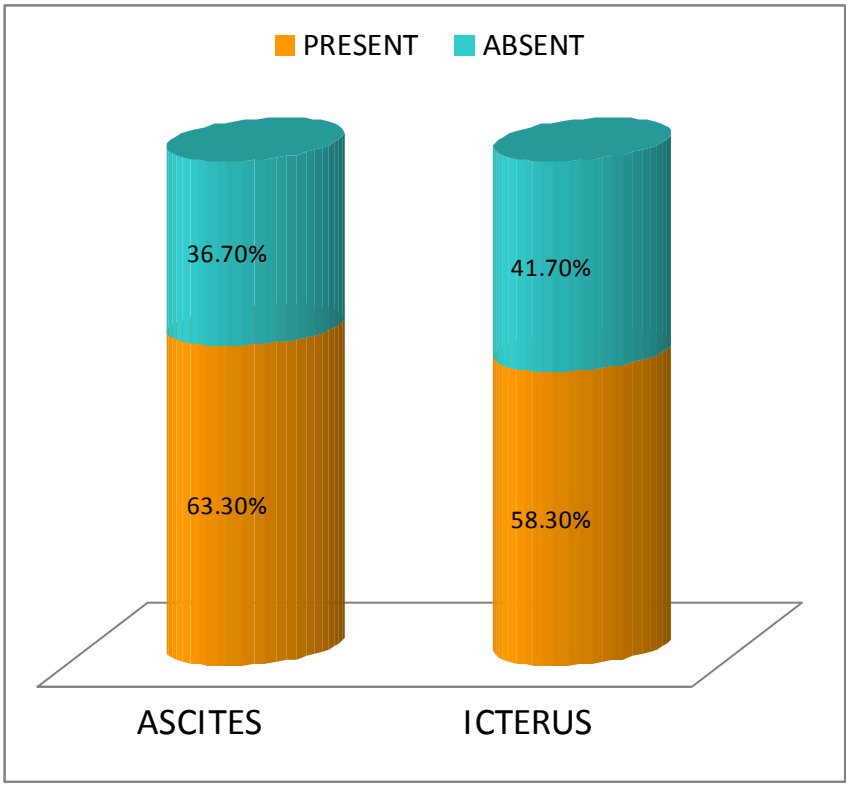
CHART 4: PIE CHART SHOWING PREVALENCE OF SPLEENOMEGALY



ASCITES AND ICTERUS:

Also, presence or absence of ascites and icterus were observed during clinical examination. It was found that 38 out of 60 patients had ascites(63.3%) while 35 out of 60 had icterus(58.3%).

CHART 5: BAR DIAGRAM SHOWING PREVALENCE OF ASCITES AND ICTERUS



OTHERS:

Clinical parameters associated with complications of varices such as encephalopathy and spontaneous bacterial peritonitis were also noted. These dramatic events were present in only 5 patients and absent in the majority(88.3%).

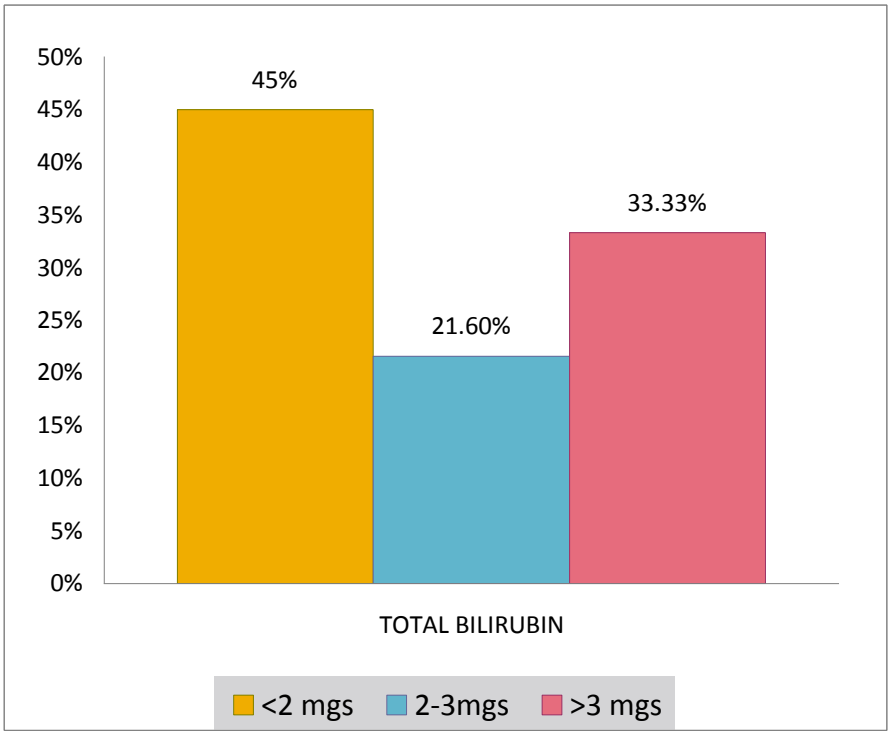
Table 7: Prevalence Of Complications Of Cirrhosis

Sl.no	Particulars	No.of respondents (n=60)	Percentage (100%)
1	Nil	53	**88.3**
2	Encephalopathy	4	**6.7**
3	SBP	1	**1.7**

BIOCHEMICAL PARAMETERS-

TOTAL BILIRUBIN

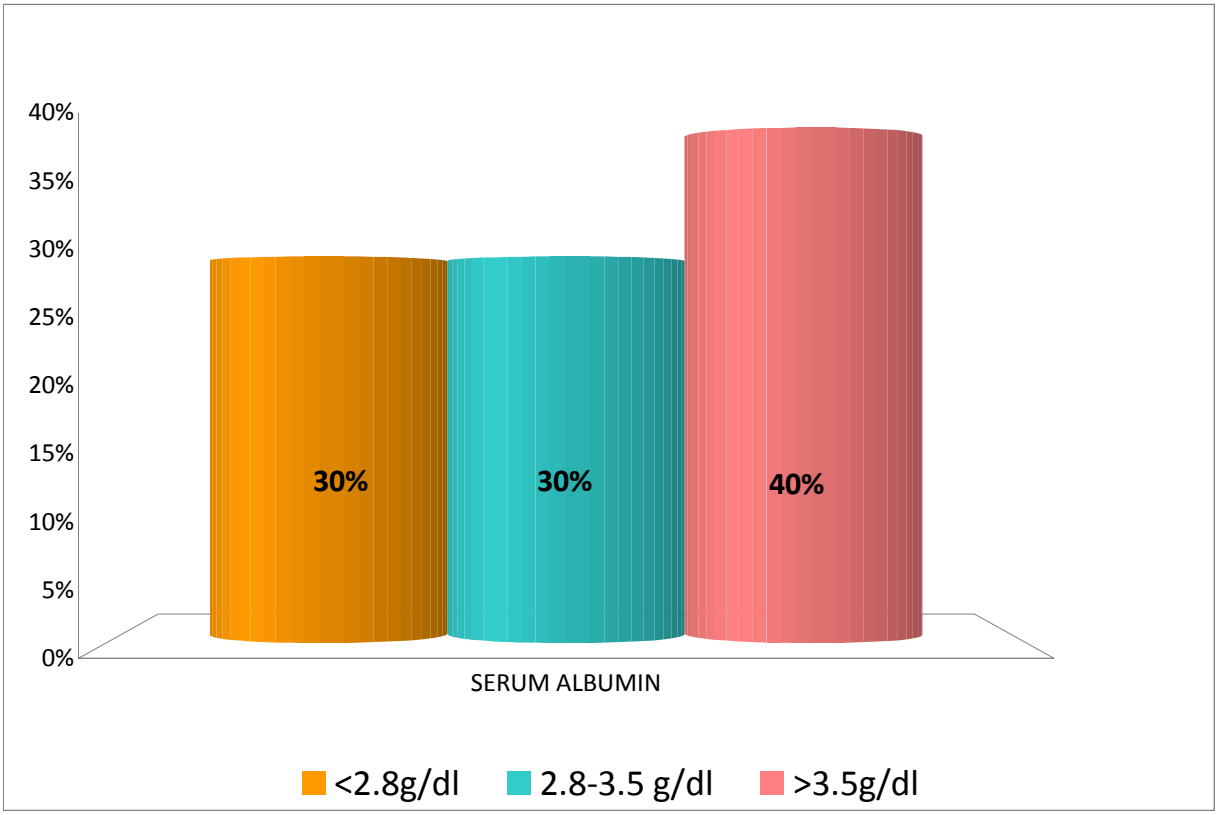
CHART 6: DISTRIBUTION OF TOTAL BILIRUBIN IN THE STUDY POPULATION



Total bilirubin was estimated in all patients, 27 out of 60(45%) had a level of <2 mg/dl, 13 patients had levels between 2-3mg/dl (21.6%) and the rest i.e. 20 patients(33.3%) had levels above 3 mg/dl. The mean total bilirubin levels were estimated to be 3.3+/- 3.07 mg/dl.

SERUM ALBUMIN:

CHART 7: DISTRIBUTION OF SERUM ALBUMIN IN THE STUDY POPULATION

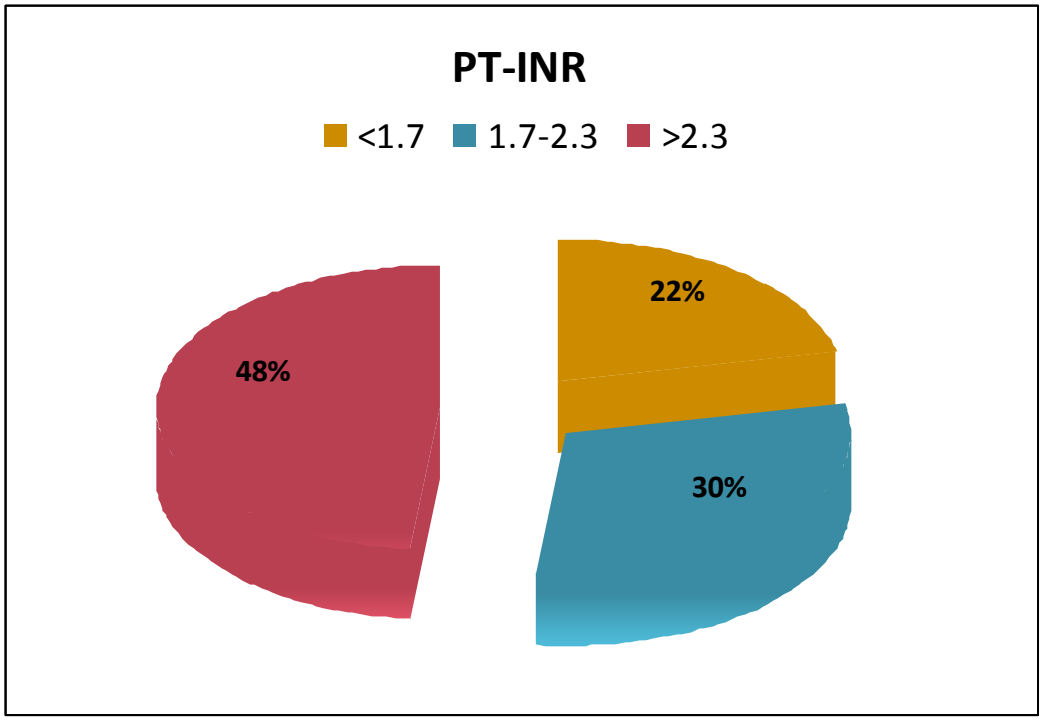


Serum albumin levels were <2.8g/dl in 30%, between 2.8-3.5 g/dl in 30% and >3.5% g/dl in 40%.

PT-INR:

PT-INR was calculated for all patients included in the study. An elevated PT-INR >2.3 was found in majority of patients (48.3%). 30% had values in between 1.7-2.3 and 21.6% had a PT-INR of less than 1.7.

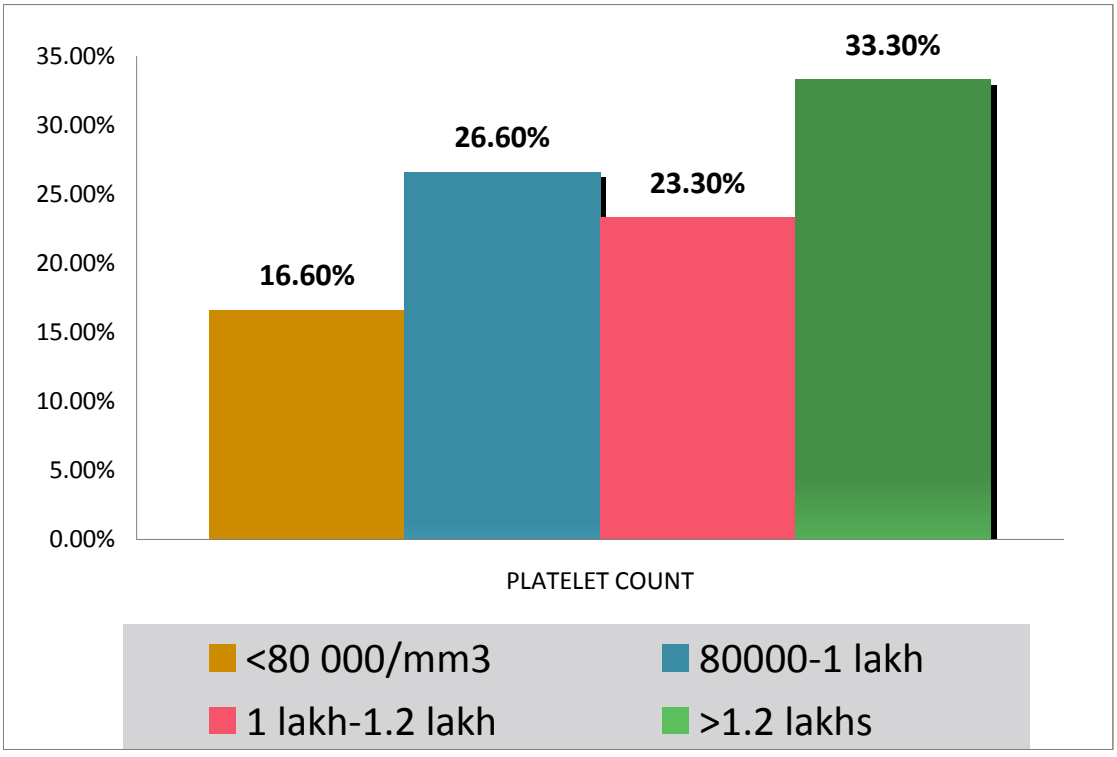
CHART 8: DISTRIBUTION OF PT-INR IN THE STUDY POPULATION



PLATELET COUNTS:

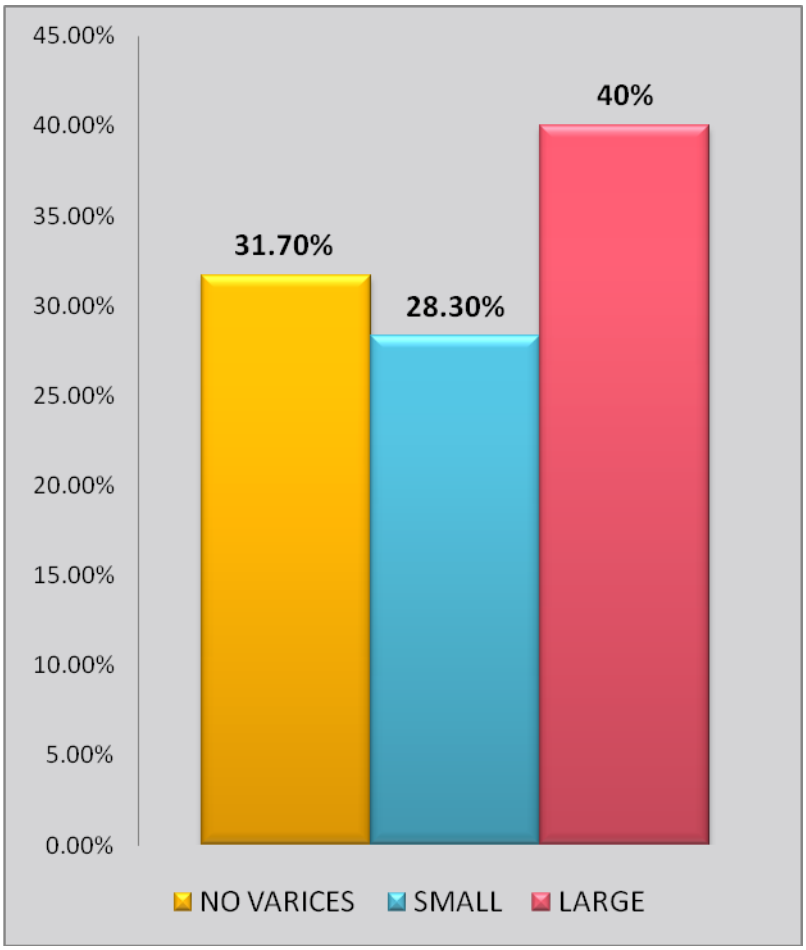
Platelet counts were obtained by automated cell counters used in our central lab and were cross checked by manual examination. They are expressed as counts/mm^3. It was found that while 33.3% had platelet count >1.2 lakhs/mm^3, only16.6% had counts <80 000/mm^3. But 37.5% patients with large varices had counts <80 000/mm^3 while only around 12% had counts over 1.2 lakhs/mm^3. This was statistically significant as depicted in table 10.

CHART 9: DISTRIBUTION OF PLATELET COUNT IN THE STUDY POPULATION



UGI SCOPY:

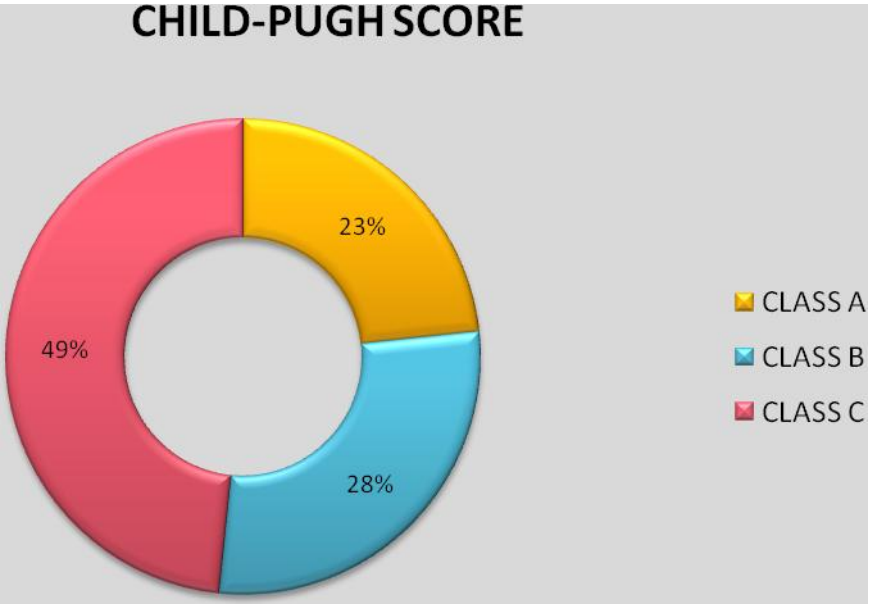
CHART 10: BAR DIAGRAM SHOWING DISTRIBUTION OF VARICES IN THE POPULATION



UGI scopy using video endoscope demonstrated the presence of large varices in 24 study patients (40%), absent varices in 19(31.7%) and small varices in 17(28.3%).

CHILD-PUGH'S SCORE:

Chart 11: pie chart showing stratification of patients according to Child-Pugh's scoring:



Child Pugh score was calculated using the five parameters- ascites, encephalopathy, total bilirubin, serum albumin and PT-INR. Patients were classified into class A, B and C respectively. 29 out of 60 patients fell in the class C, accounting for 48.3%, class B had 28.3% and class A constituted 23.3% of all patients. Hence the largest population was of patients with decompensated disease.

PLATELET COUNT / SPLEEN DIAMETER RATIO

Based on data collected, a platelet count/spleen diameter cut off of 909 was applied in this study. 41 patients out of 60 had a ratio <909(70%) and the other 19 had a ratio of >909(30%)

CHART 12:

DISTRIBUTION OF PATIENTS WITH PSR CUTOFF OF 909

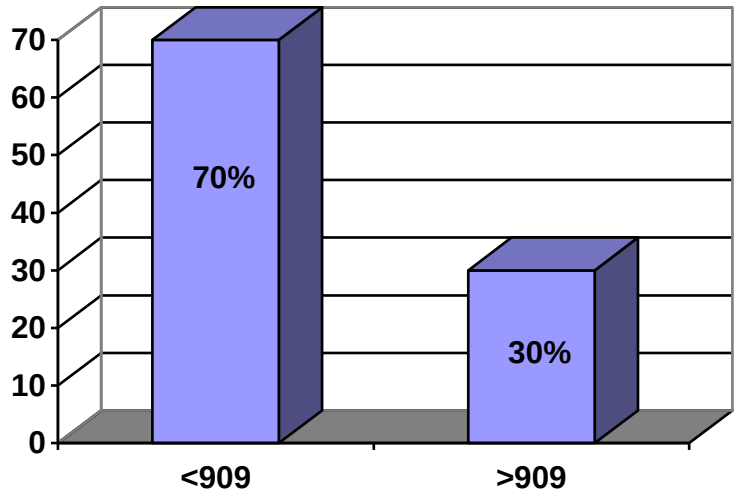


TABLE 8: DESCRIPTIVE STATISTICS:

Item	n	Min.	Max.	Mean	S.D.
Age	60	16	65	40.48	12.043
Total bilirubin	60	.80	15.20	3.3367	3.07455
AST	60	25	560	199.07	130.968
ALT	60	22	555	158.73	119.248
Serum albumin	60	1.00	5.50	3.3233	1.06044
PT-INR	60	1.00	4.00	2.3680	.77854
Splenomegaly(USG)	60	100	180	139.70	15.938
PSR	60	375.00	1500.00	842.3748	260.39289

From statistical analysis of data obtained from the study, the average age of a patient with cirrhosis in this group was 40.48 with a SD (standard deviation) of 12.04. The mean spleen size on ultrasound was 139.7mms (123-157). The mean PSR was 842.37 with a SD of 260.39.

Table 9: Oneway ANOVA difference between UGI Scopy of the respondents and their Platelet Count/Splenic Diameter

Sl.no	Platelet Count/Splenic Diameter	Mean	S.D	SS	Df	MS	Statistical inference
1	Between Groups			2938461.468	2	1469230.734	F=78.857 .000<0.05 Significant
	No varices (n=19)	1158.66	136.304				
	Small (n=17)	769.35	107.954				
	Large (n=24)	643.7108	153.380				
2	Within Groups			1062001.547	57	18631.606	

Statistical test: *Oneway ANOVA 'f' test was used the above table*

The above table inferred that there is a significant difference between UGI Scopy of the respondents(between and within groups) and their PSR. Hence, the calculated value less than table value *(.000<0.05)*.

Karl Pearson coefficient correlation test was used to compare PSR with other non invasive parameters described in the diagnosis of varices. It was found there was no significant correlation between PSR and total bilirubin, SGOT and SGPT ($p>0.05$).

But a significant relationship was found between PSR with presence of ascites, low platelet counts, spleen diameter on ultrasonography, PT-INR and child Pugh's scores ($p<0.05$).

Table 10: Association between Age, Sex, Etiology, Splenomegaly, Ascites, Icterus, Others, Platelet count, Child's score of the respondents and their UGI Scopy

Variables	UGI Scopy						Statistical inference
	No variation		Small		Large		
	(n=19)	*(100%)*	*(n=17)*	*(100%)*	*(n=24)*	*(100%)*	
Age							
Below 25yrs	4	21.1%	2	11.8%	1	4.2%	X^2=3.109 Df=4 .540>0.05 Not Significant
26 to 50yrs	11	57.9%	11	64.7%	18	75.0%	
51yrs & above	4	21.1%	4	23.5%	5	20.8%	
Sex							
Male	12	63.2%	12	70.6%	17	70.8%	X^2=.344 Df=2 .842>0.05 Not Significant
Female	7	36.8%	5	29.4%	7	29.2%	
Etiology							
Alcoholic	10	52.6%	7	41.2%	13	54.2%	X^2=11.202 Df=10 .342>0.05 Not Significant
Alcohol +	0	.0%	3	17.6%	3	12.5%	
Viral Hepatitis	2	10.5%	4	23.5%	5	20.8%	
Wilson's	2	10.5%	1	5.9%	1	4.2%	
Cryptogenic	5	26.3%	1	5.9%	1	4.2%	
Autoimmune	0	.0%	1	5.9%	1	4.2%	
Splenomegaly							
No	11	57.9%	4	23.5%	2	8.3%	X^2=16.123 Df=4 .003<0.05 Significant
Mild	6	31.6%	8	47.1%	9	37.5%	
Moderate	2	10.5%	5	29.4%	13	54.2%	
Ascites							
No	12	63.2%	3	17.6%	7	29.2%	X^2=8.971 Df=2 .011<0.05 Significant
Yes	7	36.8%	14	82.4%	17	70.8%	
Icterus							
No	9	47.4%	7	41.2%	9	37.5%	X^2=.427 Df=2 .808>0.05 Not Significant
Yes	10	52.6%	10	58.8%	15	62.5%	

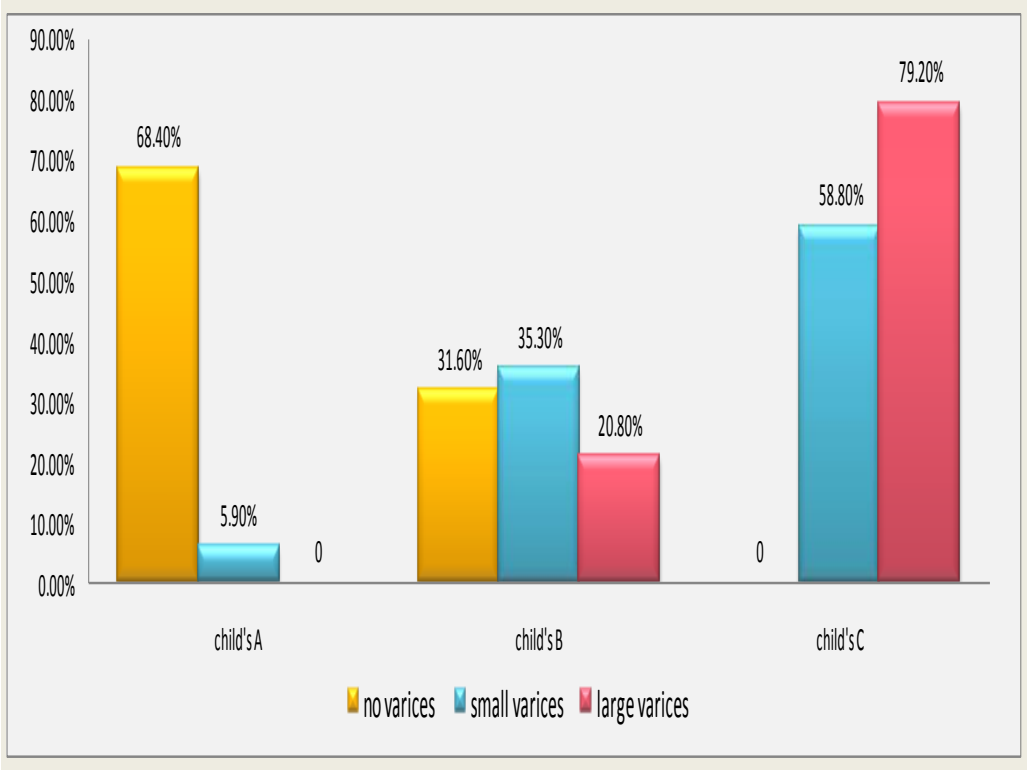
Others							
Nil	19	100.0%	15	88.2%	19	79.2%	X^2=8.558 Df=6 .200>0.05 Not Significant
Encephalopathy	0	.0%	1	5.9%	3	12.5%	
SBP	0	.0%	1	5.9%	0	.0%	
Platelet count							
Below 80000	0	.0%	1	5.9%	9	37.5%	X^2=38.223 Df=6 .000<0.05 Significant
80001 to 1lk	2	10.5%	9	52.9%	7	29.2%	
1lk to 1.2lk	1	5.3%	5	29.4%	5	20.8%	
More than 1.2lk	16	84.2%	2	11.8%	3	12.5%	
Child's score							
A	13	68.4%	1	5.9%	0	.0%	X^2=39.501 Df=4 .000<0.05 Significant
B	6	31.6%	6	35.3%	5	20.8%	
C	0	.0%	10	58.8%	19	79.2%	
PSR							
Below 909	0	0	15	88.2%	24	100.0%	X^2=55.489 Df=2 .000<0.05 Significant
Above 909	19	100%	2	11.764%	0	.0%	
Total Bilirubin							
< 2	10	52.6%	7	41.2%	10	41.7%	X^2=4.839 Df=4 .304>0.05 Not Significant
2 to 3	6	31.6%	2	11.8%	5	20.8%	
> 3	3	15.8%	8	47.1%	9	37.5%	
Serum Albumin							
< 2.8	0	.0%	7	41.2%	12	50.0%	X^2=35.821 Df=4 .000<0.05 Significant
2.8 to 3.5	1	5.3%	8	47.1%	8	33.3%	
> 3.5	18	94.7%	2	11.8%	4	16.7%	
PT-INR							
< 1.7	11	57.9%	1	5.9%	1	4.2%	X^2=27.946 Df=4 .000<0.05 Significant
1.7 to 2.3	7	36.8%	6	35.3%	6	25.0%	
> 2.3	1	5.3%	10	58.8%	17	70.8%	

Statistical test: *Chi-square test was used the above table*

The Chi square test was used to study the association of various variables with the presence of oesphageal varices on UGI scopy and the results so obtained are documented in the above table. The following inferences were drawn: there was no significant association between Age, Sex, Etiology, Icterus, total bilirubin levels of the patients and their UGI Scopy. A significant association was found between Splenomegaly, Ascites, Platelet count, serum albumin, PT-INR, Child Pugh's score and Platelet Count/Spleen diameter of the respondents and their UGI SCOPY. Hence, the calculated value less than table value *(.P<0.05)*. This demonstrates that PSR can be used in par with the other well known parameters in aiding non invasive diagnosis of OVs.

CHART 13

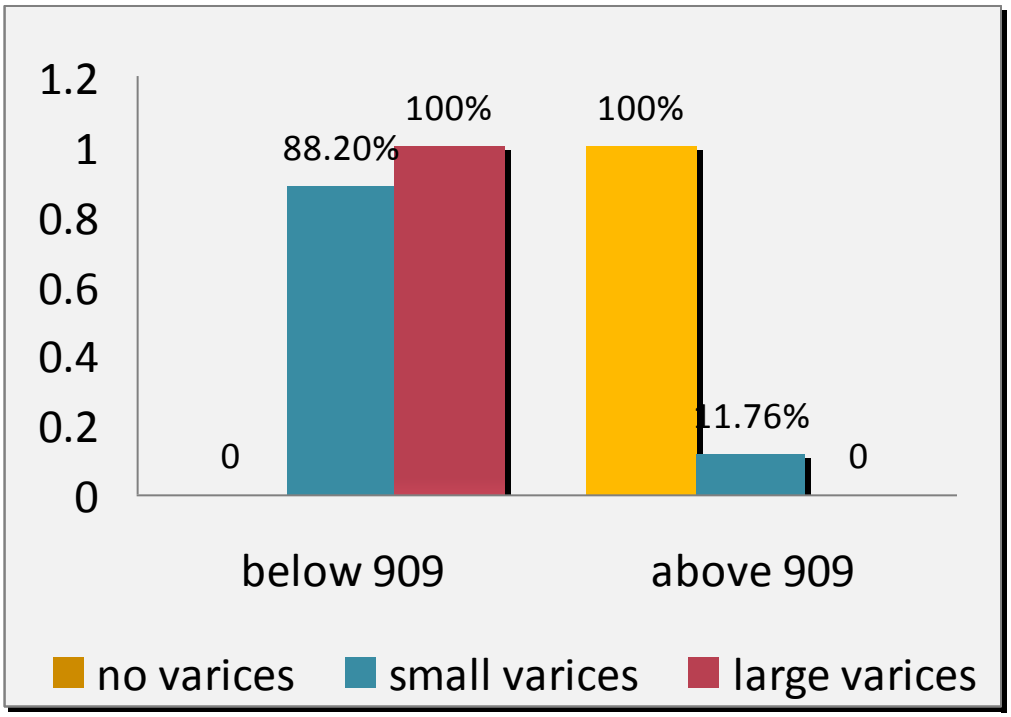
BAR DIAGRAM DEPICTING ASSOCIATION OF VARICES WITH CHILD-PUGH'S SCORE:



The above chart depicts the association of grades of varices as observed by UGI scopy with the Child-Pugh's class among the study population. It shows that 79.2% patients with large varices belonged to class C while 20.8% belonged to class B. patients in class A did not have large varices. While 68.4% of patients in the no-varices group belonged to class A, 31.6% belonged to class B and none were found in class C. This suggests that the prevalence of oesophageal varices increases with higher Child-Pugh's class, although a clear cut off is difficult to obtain.

PSR vs. UGI scopy:

CHART 14: BAR DIAGRAM SHOWS THE RELATIONSHIP BETWEEN PSR AND VARICES



When the association of PSR with grades of varices as diagnosed and graded by UGI scopy was studied, it was found that all patients with large varices had a PSR<909 and all patients with no varices had PSR>909. Interestingly, 15 out of 17 patients with small varices had a PSR<909(88.2%) while the other 2 had a ratio of >909(11.8%). This shows that while a PSR cutoff of 909 accurately predicted the absence of varices and large varices, in prediction of small varices it was less accurate.

SENSITIVITY AND SPECIFICITY

TABLE 11: SENSITIVITY AND SPECIFICITY OF PSR AS A DIAGNOSTIC TOOL

	Estimated Value	95% Confidence Interval	
		Lower Limit	Upper Limit
Prevalence	0.7	0.566268	0.807996
Sensitivity	0.952381	0.82576	0.991709
Specificity	0.888889	0.639269	0.980517

Upon consolidation of all the obtained data, PSR showed a sensitivity of 95.2% and specificity of 88.8%. Prevalence adjusted positive predictive value of the test was found to be 95% and negative predictive value of 89%.

DISCUSSION

In this study conducted during a 1 year period, 60 newly diagnosed cases of liver cirrhosis were included. Patients with unstable vitals at admission, history of variceal bleeds or treatment (medical or surgical) were excluded from the study.

Out of these 60 patients, 41(68.3%) were males and 19(31.7%) were females. A male predominance is probably because of increased incidence of alcohol abuse and alcohol related liver disease in this population.

The highest number of patients was found to be between ages 25-50 yrs (66.7%). While ages above 51 yrs constituted 21.7%, and below 25 yrs constituted of 11.7% of the study population. The mean age was found to be 40.48 yrs.

No age or sex difference was observed between patients with oesophageal varices (small and large) and group with no oesophageal varices, which is comparable with results obtained by **E Giannini et al**.[1]

Alcoholic cirrhosis accounted for highest number of cases; 30 out of 60 patients' i.e 50% of the study group. Also coexisting viral hepatitis was identified in 6 patients. Both Hepatitis B and C are well known to accelerate the progression of liver disease and precipitate decompensation in alcoholic cirrhosis. Evidence of viral hepatitis was found in 18.3% patients, forming

the second largest group with cirrhosis. Wilson's disease diagnosed by serum ceruloplasmin levels, KF rings and urinary copper excretion tests was found in 4(6.7%) patients. It is noteworthy that all these patients were <21 yrs of age, implicating that Wilson's disease is a cause for early onset hepatocellular degeneration. 2 cases of autoimmune disease (3.3%) related cirrhosis were encountered. 7 cases had no identifiable etiology and were classified as cryptogenic (11.7%). This is comparable with etiological distribution shown in other studies**. Chang M H and colleagues**[85] found that in a study group of 736 patients in 42.4% of liver cirrhosis was due to chronic alcoholism, closely followed by viral hepatitis (41.2%). Though there is a predominance of alcohol related cirrhosis in our study as well, a difference in incidence of viral hepatitis between the two studies maybe due to the larger study population in the latter study.

On clinical examination, important markers of portal hypertension and decompensated liver disease were concentrated upon. These were splenomegaly, ascites and icterus. As in this population spider naevi are difficult to discern they were not included in the study despite their association with portal hypertension as demonstrated in other studies.

17 patients in the study group had no palpable spleen on examination, constituting 28.3% of the study population. Majority of the patients had mild splenomegaly; 23 out of 60(38.3%). While moderate spleen was seen

in 33.3%. Massive splenomegaly (spleen palpable beyond the umbilicus) was not recorded in this study. 54.2% patients with large varices had moderate splenomegaly while only 8.3% has no splenomegaly. This suggests a strong correlation between spleen size and presence of oesophageal varices ($p<0.005$). Association of splenomegaly with presence of oesophageal varices has been well demonstrated by studies like **Thomopoulos et al**[9] and **Chang M H and colleagues**[85].

Icterus observed in 35 out 60 patients (58.3%) though the correlation between oesophageal varices and presence of icterus was found to be insignificant statistically in our study. While 62.5% patients with large varices had icterus, 52.6% with no oesophageal varices also had icterus. However, **Thomopoulos et al**[9] demonstrated serum bilirubin ($p = 0.01$) as one of the variables associated with presence of varices on univariate analysis. But they failed to show any significance between the two on multivariate analysis.

Ascites was recorded in 68.3% of the study population. Over 70.8% cases with large varices had ascites, while 63.2% patients with absent varices had no ascites. The relationship between presence of varices and ascites has been found to be statistically significant in our study. **Ng FH et al**[10] concluded in their study that endoscopic screening for varices were not necessary until ascites or thrombocytopenia occurred. **Chang MH et al**[85]

concluded in their study that patients who have at least two among ascites, splenomegaly, and alcoholism would have an increased risk of having large esophageal varices . This was also supported by **Thomopoulos et al[9].**

It is noteworthy that a few patients also had advanced complications of portal hypertension such as spontaneous bacterial peritonitis(SBP) and hepatic encephalopathy. Although no significant correlation between these and presence of oesophageal varices was found in our study. However, in study by **Ng FH et al[10]**, patients with hepatic encephalopathy were found to be significantly associated with presence of varices.

Platelet counts have been independently associated with oesophageal varices in patients with chronic liver disease and this has been demonstrated by a multitude of studies.[1, 7,9,10,54].Reduced platelet counts in liver disease may depend on factors other than portal hypertension, such as decreased thrombopoietin production, reduced mean platelet survival or myelotoxic effects of alcohol or hepatitis viruses. And hence, though there is a significant association it has low specificity.

Pilette C et al[7] concluded in their study that at a diagnostic threshold of 160 G/L counts, a sensitivity of 80% and a specificity of 58% was obtained. Platelet count ≥260 G/I had a negative predictive value ≥91%. **Zaman A and colleagues[86]** concluded that a platelet count of <88,000 was the only parameter identified by univariate/multivariate analysis ($p < 0.05$)

as associated with the presence of large esophageal varices (odds ratio 5.5; 95% confidence interval 1.8-20.6) or gastric varices (odds ratio 5; 95% confidence interval 1.4-23). Platelet count < 90,000/ μl was found to be significantly associated with large varices as demonostrated by **Jijo V Cherian and colleagues**[54] (OR 2.7; 95% CI, 1.4 – 5.2).

A platelet count of <80 000 was seen in only 16.7% and was associated with large varices in 37.5% which was significant. On the other hand only 12.5% of patients with large varices had a count of above 1.2 lakhs(35%), while 84.2% had no varices. This finding correlates with other studies wherein thrombocytopenia has shown to be associated with varices, but a definitive cutoff level is difficult to obtain.

Patients with large varices had a mean total bilirubin level of 3.6md/dl, while those with no varices had mean total bilirubin of 2.77. There was no significant correlation between the two parameters in this study. Although some studies have demonstrated an association[9]

There was no significant correlation between AST and ALT with the presence of varices, and this is in accordance with studies by **Giannini et al**[1]

On the other hand parameters like serum albumin and PT-INR showed significant associations ($p<0.05$). Patients with large varices had

lower mean serum albumin levels (2.7g/dl) and elevated PT-INR(2.8) as demonstrated by **Bressler B, Pinto R, El-Ashry D, Heathcote EJ**[12] in their study.

All patients in this study were stratified into Child Pugh's class, which is also an independent non invasive predictor of oesophageal varices in cirrhotics. Majority of the patients, 29 out of 60 fell in class C(48.3%), followed by class B(28.3%) and class A(23.3%). The correlation of Child's scoring and presence of oesophageal varices was found significant in this study. Patients with higher Child-Pugh's class were found to have large varices. None of the patients with large varices belonged to class A while 79.2% of the cases fell in class C. In a study conducted by **Jijo V Cherian and colleagues**[54], Child-Pugh class B/C were found to be associated with higher grades of varices, which is comparable with our study.

On UGI scopy, 31.7% patients had no varices and 68.3% showed the presence of varices (28.3% -small varices, 40%-large varices).

Platelet count/spleen diameter was calculated for all patients. 42 patients had a ratio of <909(70%), and 18 had a ratio of >909(30%). Platelet count was found to be significantly associated with clinical parameters like ascites and splenomegaly, laboratory parameters like serum albumin and PT-INR and radiologically with spleen diameter. But no association was found with total bilirubin and the liver enzymes.

Significant association was found between presence of varices and the platelet count/spleen diameter. Studies by **Giannini et al**[1]and **Baig WW and colleagues**[13] also demonstrated that PSR has high accuracy in predicting varices non invasively. However, in the study by Baig WW a PSR cut off of 1014 was employed and found to have a positive predictive value of 95.4% and negative predictive value of 95.1%[13].

A platelet count-spleen diameter ratio of ≤ 666 was significantly associated with the presence of oesophageal varices in a predominant alcohol related cirrhosis subset when studied by **Jijo V Cherian and colleagues**[54]. This ratio was found insignificant on multivariate analysis.

In this study, all patients with large varices had a ratio <909 and all patients with no varices had a ratio>909. However, 11.8% patients with small varices had a PSR >909. This denotes that while PSR at a cut off of 909 accurately predicts absence of varices or large varices, small varices were missed in 2 cases.

The sensitivity and specificity of this test in non invasively predicting oesophageal varices is 95.2% and 88.9% respectively, which is comparable with the results of the meta-analysis by **Ying L et al**[14]. The prevalence adjusted positive predictive value was 95% and the negative predictive value was 89%.

CONCLUSION

1. Platelet count/spleen diameter is valuable tool in non invasive prediction of oesophageal varices in patients with cirrhosis.

2. Platelet count/spleen diameter was independently associated with presence of oesophageal varices on UGI scopy.($p<0.05$)

3. Platelet count/spleen diameter was also found to strongly correlate with other non invasive diagnostic tools like ascites, splenomegaly, platelet count, serum albumin, PT-INR and Child Pugh's score.

4. It had a sensitivity of 95.2% and specificity of 88.9% in predicting oesophageal varices in patients with cirrhosis when a cut off 909 was applied.

5. Platelet count/spleen diameter had a prevalence adjusted positive predictive value of 95% and prevalence adjusted negative predictive value of 89%.

6. To some extent, this parameter also helps predict large and small varices. The ratio being smaller in patients with larger varices. Although further studies are required for validation of this and for detecting valid cut off ratios.

7. The use of platelet count/spleen diameter ratio would avoid unnecessary endoscopy in patients with cirrhosis without a significant risk of missing oesophageal varices.

8. Platelet count/spleen diameter ratio can be calculated easily, is reproducible and less cumbersome than UGI scopy.

9. In a rural setup where UGI scopy may not be possible, platelet count/spleen diameter may be of help to the physicians in helping initiate appropriate primary pharmacological prophylaxis in these patients.

10. In urban settings where endoscopic workload is high, this non invasive predictor can help to initiate drug therapy while waiting for the endoscopy procedure.

References:

1. Giannini E, Botta F, Borro P, Risso D, Romagnoli P, Fasoli A, et al. PSR: Proposal and validation of a non-invasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis. Gut. 2003;52:1200–5

2. Garceau AJ, Chalmers TC. The Boston Inter-Hospital Liver Group. The natural history of cirrhosis: I. Survival with OV. *N Engl J Med*1963;268:469–73.

3. Graham D, Smith JL. The course of patients after variceal hemorrhage.*Gastroenterology*1981;80;800–9.

4. Rigo GP, Merighi A, Chalen JN, *et al.* A prospective study of the ability of three endoscopic classifications to predict hemorrhage from OV. *Gastrointest Endosc*1992;38:425–9

5. D'Amico G, Garcia-Tsao G, Calés P, *et al.* Diagnosis of portal hypertension: how and when. In: De Franchis R, ed. *Proceedings of the Third Baveno International Consensus Workshop on Definitions, Methodology and Therapeutic Strategies*. Oxford: Blackwell Science 2001;36–63

6. Grace ND, Groszmann RJ, Garcia-Tsao G, *et al.* Portal hypertension and variceal bleeding: an AASLD single topic symposium. *Hepatology*1998;28:868–80.

7. Pilette C, Oberti F, Aube C, Rousselet MC, Bedossa P, Gallois Y. Non-invasive diagnosis of esophageal varices in chronic liver diseases. J Hepatol. 1999;31:867–73.

8. Chalasani N, Imperiale TF, Ismail A, Sood G, Carey M, Wilcox CM, et al. Predictors of large esophageal varices in patients with cirrhosis. Am J Gastroenterol. 1999;94:3285–91.

9. Thomopoulos KC, Labropoulou-Karatza C, Mimidis KP, Katsakoulis EC, Iconomou G, Nikolopoulou VN. Non-invasive predictors of the

presence of large oesophageal varices in patients with cirrhosis. Dig Liver Dis. 2003;35:473–8

10..Ng FH, Wong SY, Loo CK, Lam KM, Lai CW, Cheng CS. Prediction of oesophagogastric varices in patients with liver cirrhosis. J Gastroenterol Hepatol. 1999;14:785–90.

11. Schepis F, Camma C, Niceforo D, Magnano A, Pallio S, Cinquegrani M, et al. Which patients with cirrhosis should undergo endoscopic screening for esophageal varices detection? Hepatology.2001;33:333–8

12. Bressler B, Pinto R, El-Ashry D, Heathcote EJ. Which patients with primary biliary cirrhosis or primary sclerosing cholangitis should undergo endoscopic screening for oesophageal varices detection. Gut. 2005;54:407–10.

13. Baig WW, Nagaraja MV, Varma M, Prabhu R. Platelet count to spleen diameter ratio for the diagnosis of esophageal varices: Is it feasible?. Can J Gastroenterol. 2008 Oct;22(10):825-8.

14. Ying L, Lin X, Xie ZL, Hu YP, Shi KQ. Performance of PSR for diagnosis of esophageal varices in cirrhosis: a meta-analysis. Dig Dis Sci. 2012 Jun;57(6):1672-81.

15. Harvey B. Lefton MD, Anthony Rosa MD, Matthew Cohen MD. Diagnosis and Epidemiology of Cirrhosis. Medical Clinics of North America - Volume 93, Issue 4 (July 2009)

16. Pan CQ, Zhang JX. Natural History and Clinical Consequences of Hepatitis B Virus Infection. *Int J Med Sci* 2005; 2(1):36-40.

17. Fattovich G, Pantalena M, Zagni I. *et al*. Effect of hepatitis B and C virus infections on the natural history of compensated cirrhosis: a cohort of 297 patients. *Am J Gastroenterology.* 2002 ;97:2886-95

18. Leandro G., Mangia A., Hui J.: Relationship between steatosis, inflammation, and fibrosis in chronic hepatitis C; a meta-analysis of individual patient data. *Gastroenterology* 130. 1636-1642.2006

19. Conn H.: Alcohol content of various beverages: all booze is created equal. *Hepatology* 12. 1252-1258.1990

20. Purcell R.H., Emerson S.U.: Hepatitis E: an emerging awareness of an old disease. *J Hepatol* 48. (3): 494-503.2008

21. Charlton M.: Non-alcoholic fatty liver disease: a review of current understanding and future impact. *Clin Gastroenterol Hepatol* 2. 1048-1058.2004

22. Bruce R Bacon: cirrhosis and its complications, chapter 308, part 14, Harrison's principles of internal medicine, 18th edition.

23. Czaja A.J.: Autoimmune liver disease. *Curr Opin Gastroenterol* 24. (3): 298-305.2008

24. Perlmutter D.H.: Alpha-1-antitrypsin deficiency: diagnosis and treatment. *Clin Liver Dis* 8. (4): 839-859.2004

25. Roberts E.A., Schilsky M.L.: Diagnosis and treatment of Wilson disease: an update. *Hepatology* 47. (6): 2089-2111.2008.

26. Adams P.C., Barton J.C.: Hemochromatosis. *Lancet* 370. (9602): 1855-1860.2007

27. Heidelbaugh J., Bruderly M.: Cirrhosis and chronic liver failure: part 1. Diagnosis and Evaluation. *Am Fam Physician* 74. 756-762.2006

28. Cohen J., Kaplan M.: The SGOT/SGPT ratio—an indicator of alcoholic liver disease. *Dig Dis Sci* 24. (11): 835-838.1979

29. Sheth S., Glamm S., Gordon F., et al: AST/ALT ratio predicts cirrhosis in patients with chronic hepatitis C virus infection. *Am J Gastroenterol* 93. 44-48.1998

30. Imperiale T., Said A., Cummings O., et al: Need for validation of clinical decision aids: use of the AST/ALT ratio in predicting cirrhosis in chronic hepatitis C. *Am J Gastroenterol* 95. (9): 2328-2332.2000

31. Croquet V., Vuillemin E., Ternisien C., et al: Prothrombin index is an indirect marker of severe liver fibrosis. *Eur J Gastroenterol Hepatol* 14. (10): 1133-1141.2002

32. Afdhal N., McHutchinson J., Brown R., et al: Thrombocytopenia associated with chronic liver disease. *J Hepatol* 48. (6): 1000-1007.2008

33. Harbin W., Robert N., Ferrucci J.: Diagnosis of cirrhosis based on regional changes in hepatic morphology: a radiological and pathological analysis. *Radiology* 135. (2): 273-283.1980

34. Ferrell L.: Liver pathology: cirrhosis, hepatitis, and primary liver tumors. Update and diagnostic problems. *Mod Pathol* 13. (6): 679-704.2000

35. Gines P., Quintero E., Arroyo V.: Compensated cirrhosis: natural history and prognostic factors. *Hepatology* 7. 122-128.1987

36. Borowsky S.A., Strome S., Lott E.: Continued heavy drinking and survival in alcoholic cirrhosis. *Gastroenterology* 80. 1405-1409.1981

37. Bruno S., Stroffolini T., Colombo M.: Sustained virological response to interferon-alpha is associated with improved outcome in HCV-related cirrhosis: a retrospective study. *Hepatology* 45. 579-587.2007

38. D'Amico G., Garcia-Tsao G., Pagliaro L.: Natural history and prognostic indicators of survival in cirrhosis: a systemic review of 118 studies. *J Hepatol* 44. 217-231.2006;

39. deFranchis R.: Evolving consensus in portal hypertension. Report of the Baveno IV consensus workshop on methadology of diagnosis and therapy in portal hypertension. *J Hepatol* 43. (1): 167-176.2005

40. Infante-Rivard C., Esnaola S., Villeneuve J.: Clinical and statistical validity of conventional prognostic factors in predicting short-term survival among cirrhotics. *Hepatology* 7. (4): 660-664.1987

41. Salerno F., Merli M., Cazzaniga M., et al: MELD score is better than Child-Pugh score in predicting 3-month survival of patients undergoing transjugular intrahepatic portosystemic shunt. *J Hepatol* 36. (4): 494-500.2002

42. Nayantara Coelho-Prabhu, MD .Patrick S. Kamath, MD Current Staging and Diagnosis of Gastroesophageal Varices. Clinics in Liver Disease - Volume 14, Issue 2 (May 2010)

43. Nagib Toubia MD ,Arun J. Sanyal MD. Portal Hypertension and Variceal Hemorrhage. Medical Clinics of North America - Volume 92, Issue 3(May 2008)

44. Sarin S., Groszmann R.T., Mosca P.: Propranolol ameliorates the development of portal-systemic shunting in a chronic murine schistosomiasis model of portal hypertension. *J Clin Invest* 87. 1032-1036.1991

45. Pinzani M., Milani S., De Franco R., et al: Endothelin 1 is overexpressed in human cirrhotic liver and exerts multiple effects on activated hepatic stellate cells. *Gastroenterology* 110. 534-548.1996

46. Garcia-Pagan J.C., Groszmann R.J., Bosch J.: Measurement of portal pressure. *Clin Gastroenterol Hepatol* 981. 2005

47. Groszmann R.J., Garcia-Tsao G., Bosch J., et al: Beta-blockers to prevent gastroesophageal varices in patients with cirrhosis. *N Engl J Med* 353. 2254-2261.2005

48. Escorsell A., Gines A., Llach J., et al: Increasing intra-abdominal pressure increases pressure, volume, and wall tension in esophageal varices. *Hepatology* 36. 936-940.2002

49. Vianna A., Hayes P.C., Moscoso G., et al: Normal venous circulation of the gastroesophageal junction. A route to understanding varices. *Gastroenterology* 93. 876.1987

50. Eisen G.M., Eliakim R., Zaman A., et al: The accuracy of PillCam ESO capsule endoscopy versus conventional upper endoscopy for the diagnosis of esophageal varices: a prospective three-center pilot study. *Endoscopy* 38. 31.2006

51. Lu Y., Gao R., Liao Z., et al: Meta-analysis of capsule endoscopy in patients diagnosed or suspected with esophageal varices. *World J Gastroenterol* 15. 1254.2009

52. Nakos G., Karagiannis S., Ballas S., et al: A study comparing tolerability, satisfaction and acceptance of three different techniques for esophageal endoscopy: sedated conventional, unsedated peroral ultra thin, and esophageal capsule. *Dis Esophagus* 22. 447-452.2009

53. Choudhuri G., Dhiman R.K., Agarwal D.K.: Endosonographic evaluation of the venous anatomy around the gastro-esophageal junction in patients with portal hypertension. *Hepatogastroenterology* 43. 1250.1996

54. Jijo V. Cherian, Nandan Deepak,[1] Rajesh Prabhu Ponnusamy, Aravindh Somasundaram, and V. Jayanthi. Non-invasive Predictors of Esophageal Varices. Saudi J Gastroenterol. 2011 Jan-Feb; 17(1): 64–68.

55. Kazemi F., Kettaneh A., N'Kontchou G., et al: Liver stiffness measurement selects patients with cirrhosis at risk of bearing large oesophageal varices. *J Hepatol* 45. 230.2006

56. Kim Y.J., Raman S.S., Yu N.C., et al: Esophageal varices in cirrhotic patients: evaluation with liver CT. *AJR Am J Roentgenol* 188. 139.2007

57. Perri R.E., Chiorean M.V., Fidler J.L., et al: A prospective evaluation of computerized tomographic (CT) scanning as a screening modality for esophageal varices. *Hepatology* 47. 1587.2008

58. Sugano S., Yamamoto K., Sasao K., et al: Daily variation of azygos and portal blood flow and the effect of propranolol administration once an evening in cirrhotics. *J Hepatol* 34. 26.2001

59. Matsuo M., Kanematsu M., Kim T., et al: Esophageal varices: diagnosis with gadolinium-enhanced MR imaging of the liver for patients with chronic liver damage. *AJR Am J Roentgenol* 180. 461.2003

60. Dagradi A.E.: The natural history of esophageal varices in patients with alcoholic liver cirrhosis. An endoscopic and clinical study. *Am J Gastroenterol* 57. 520.1972

61. Idezuki Y.: General rules for recording endoscopic findings of esophagogastric varices (1991). Japanese Society for Portal Hypertension. *World J Surg* 19. 420.1995.

62. Brocchi E., Caletti G., Brambilla G., et al: Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. A prospective multicenter study. *N Engl J Med* 319. 983.1988

63. Rigo G.P., Merighi A., Chahin N.J., et al: A prospective study of the ability of three endoscopic classifications to predict hemorrhage from esophageal varices. *Gastrointest Endosc* 38. 425.1992

64. Cales P., Oberti F., Bernard-Chabert B., et al: Evaluation of Bavenorecommendations for grading esophageal varices. *J Hepatol* 39. 657.2003

65. D'Amico G., Pagliaro L., Bosch J.: Pharmacological treatment of portalhypertension: an evidence-based approach. *Semin Liver Dis* 19. 475-505.1999

66. Fiorucci S., Antonelli E., Morelli O., et al: NCX-1000, a NO-releasing derivative of ursodeoxycholic acid, selectively delivers NO to the liver and protects against development of portal hypertension. *Proc Natl Acad Sci U S A* 98. 8897-8902.2001

67. Prophylactic sclerotherapy for esophageal varices in men with alcoholic liver disease: a randomized, single-blind, multicenter clinical trial. The Veterans Affairs Cooperative Variceal Sclerotherapy Group. *N Engl J Med* 324. 1779-1784.1991

68. Imperiale T.F., Chalasani N.: A meta-analysis of endoscopic variceal ligation for primary prophylaxis of esophageal variceal bleeding. *Hepatology* 33. 802-807.2001

69. Kravetz D., Bosch J., Arderiu M., et al: Hemodynamic effects of blood volume restitution following a hemorrhage in rats with portal hypertensiondue to cirrhosis of the liver: influence of the extent of portal-systemic shunting. *Hepatology* 9. 808-814.1989

70. Bosch J., Thabut D., Bendtsen F., et al: Recombinant factor VIIa for upper gastrointestinal bleeding in patients with cirrhosis: a randomized, double-blind trial. *Gastroenterology* 127. 1123-1130.2004

71. Goulis J., Armonis A., Patch D., et al: Bacterial infection is independently associated with failure to control bleeding in cirrhotic patients with gastrointestinal hemorrhage. *Hepatology* 27. 1207-1212.1998

72. Bernard B., Grange J.D., Khac E.N., et al: Antibiotic prophylaxis for the prevention of bacterial infections in cirrhotic patients with ascites: a meta-analysis. *Digestion* 59. (Suppl 2): 54-57.1998

73. Escorsell A., Ruiz del Arbol L., Planas R., et al: Multicenter randomized controlled trial of terlipressin versus sclerotherapy in the treatment of acute variceal bleeding: the TEST study. *Hepatology* 32. 471-476.2000

74. Bosch J., Kravetz D., Rodes J.: Effects of somatostatin on hepatic and systemic hemodynamics in patients with cirrhosis of the liver: comparison with vasopressin. *Gastroenterology* 80. 518-525.1981

75. Cales P., Masliah C., Bernard B., et al: Early administration of vapreotide for variceal bleeding in patients with cirrhosis. *N Engl J Med* 344. 23-28.2001

76. D'Amico G., Pietrosi G., Tarantino I., et al: Emergency sclerotherapy versus vasoactive drugs for variceal bleeding in cirrhosis: a Cochrane meta-analysis. *Gastroenterology* 124. 1277-1291.2003

77. D'Amico G., Pagliaro L., Bosch J.: The treatment of portalhypertension: a meta-analytic review. *Hepatology* 22. 332-354.1995

78. Cook D., Laine L.: Indications, technique, and complications of balloon tamponade for variceal gastrointestinal bleeding. *J Intensive Care Med* 7. 212-218.1992

79. Azoulay D., Castaing D., Majno P., et al: Salvage transjugular intrahepatic portosystemic shunt for uncontrolled variceal bleeding in patients with decompensated cirrhosis. *J Hepatol* 35. 590-597.2001

80. Malinchoc M., Kamath P.S., Gordon F.D., et al: A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. *Hepatology* 31. 864-871.2000

81. Graham D.Y., Smith J.L.: The course of patients after variceal hemorrhage. *Gastroenterology* 80. 800-809.1981

82. de Franchis R., Primignani M.: Why do varices bleed?. *Gastroenterol Clin North Am* 21. 85-101.1992

83. Luca A., D'Amico G., La Galla R., et al: TIPS for prevention of recurrent bleeding in patients with cirrhosis: meta-analysis of randomized clinical trials. *Radiology* 212. 411-421.1999

84. Meddi P., Merli M., Lionetti R., et al: Cost analysis for the prevention of variceal rebleeding: a comparison between transjugular intrahepatic portosystemic shunt and endoscopic sclerotherapy in a selected group of Italian cirrhotic patients. *Hepatology* 29. 1074-1077.1999

85. Chang MH, Sohn JH, Kim TY, Son BK, Kim JP, Jeon YC, Han DS. Non-endoscopic predictors of large esophageal varices in patients with liver cirrhosis. Korean J Gastroenterol. 2007 Jun;49(6):376-83

86. Zaman A, Hapke R, Flora K, Rosen HR, Benner K. Factors predicting the presence of esophageal or gastric varices in patients with advanced liver disease .Am J Gastroenterol. 1999 Nov;94(11):3292-6.

S.No	NAME	AGE	SEX	IP NUMBER	ETIOLOGY	SPLENOMEGALY	ASCITES	ICTERUS	OTHERS	TOTAL BILIRUBIN	AST	ALT	SERUM ALBUMIN	PT-INR	PLATELET COUNT	SPLENOMEGALY(USG)	PSR	UGI SCOPY	CHILD'S SCORE
1	Basheer ahmed	53	male	1379696	alcoholic	3cms	+	+		5.4	210	120	2	2.8	80 000	150	533	large	C
2	vijay kumar	35	male	1379681	alcoholic	no	+	+		6	145	120	3.4	2.4	80 000	120	666	small	C
3	vasugi	33	female	1366121	cryptogenic	3 cms	no	no		1.4	124	150	4.5	1.6	1.5 lakhs	140	1071.4	NO VARICES	A
4	prabhakaran	50	male	1386978	alcoholic	no	no	+		2.8	145	50	4.5	1.4	1.4 lakhs	120	1250	NO VARICES	A
5	valiyapathy	55	female	1388177	hepatitis B	5 cms	+	no		0.9	70	56	1.8	2.8	90 000	160	562.5	small	C
6	arul doss	55	male	1388190	alcoholic	2 cms	+	no		1.1	160	100	3	2.8	1.3 lakhs	150	866.6	large	B
7	muthaiyya	42	male	1388210	alcoholic,	4cms	+	no		1.1	145	110	1.4	3.08	1.1 lakhs	150	733.33	large	C
8	kaliyaperumal	48	male	1388612	alcoholic	4cms	+	+		2.8	245	145	3	3	80 000	154	519.4	large	C
9	muthalakshmi	50	female	1320576	cryptogenic	no	+	no		0.8	25	22	4	2.8	1 lakh	130	769	large	B
10	kannan	32	male	1312517	alcoholic,	2 cms	+	+		5.8	97	128	4.5	3	1.3 lakhs	142	915.5	small	C
11	selvam	40	male	1315981	alcoholic	2 cms	+	no		1.1	78	55	2.7	1.4	88 000	145	606.9	small	B
12	panchabhikesha	59	male	1383465	hepatitis B	no	+	no		0.8	126	57	2.4	3	1 lakh	130	769.2	small	B
13	manimeghalai	20	female	1383313	wilson's	3 cms	no	no		1.1	56	45	2.3	1.8	1.12 lakhs	150	746.6	large	B
14	dhanamani	30	female	1383283	autoimmune	2cms	no	no		1.1	345	469	3.4	2.1	1.1 lakhs	150	733.33	large	B
15	vanita	33	female	1383306	hepatitis B	2 cms	no	no		1.2	200	137	2.4	1.6	80 000	150	533	large	B
16	santhappan	53	male	1380291	alcoholic	no	+	no		1.2	234	143	4	1.9	1.43 lakhs	135	1059.2	NO VARICES	A
17	shivaranjini	21	female	1383667	wilson's	1	no	no		0.8	68	55	4	2.1	1.3 lakhs	124		NO VARICES	A
18	muthukannu	33	male	1382462	alcoholic	no	+	+		2.4	234	170	4	2	1.5 lakhs	110	1363.6	NO VARICES	B
19	lakshmi	60	female	1383657	hepatitis B	2 cms	+	+		3	120	35	2	2.6	1 lakhs	130	769	large	C
20	ali batcha	40	male	1354177	alcoholic	2 cms	+	+		11.8	450	260	1	3.8	66 000	148	445.9	large	C
21	nagamani	54	male	1384420	alcoholic	no	no	+		10.4	555	400	3.5	1.6	1.6 lakhs	120	1333.3	NO VARICES	B
22	malliga	47	female	1384781	autoimmune	2 cms	+	no		1.2	280	200	3	2	1.2 lakhs	140	857.14	small	B
23	sathish kumar	16	male	1377289	wilson's	no	no	no		1.2	29	31	4.5	1.2	1.8 lakhs	120	1500	NO VARICES	A
24	kannaiyan	40	male	1384777	alcoholic	6 cms	+	no		1.4	120	98	2	2.4	1.4 lakhs	170	823.5	small	C
25	murugeshan	45	male	1385616	alcoholic	2 cms	+	+		8.2	230	140	3.8	2.8	1.1 lakhs	140	785.7	large	C

S.No	NAME	AGE	SEX	IP NUMBER	ETIOLOGY	SPLENOMEGALY	ASCITES	ICTERUS	OTHERS	TOTAL BILIRUBIN	AST	ALT	SERUM ALBUMIN	PT-INR	PLATELET COUNT	SPLENOMEGALY(USG)	PSR	UGI SCOPY	CHILD'S SCORE
26	irulambal	50	female	1388106	cryptogenic	6 cms	+	no		0.8	120	100	3.6	1.8	1.8 lakhs	170	1058.8	NO VARICES	B
27	sivasamy	35	male	1385745	alcoholic	5 cms	no	+		3.8	340	200	4	2.5	1.0 lakh	160	625	large	C
28	Mohd. Amanulla	40	male	1385482	alcoholic	no	+	+		1.8	268	200	4.8	1.4	1.35 lakhs	120	1125	NO VARICES	A
29	durai	50	male	1383772	alcoholic	4 cms	+	+		2.2	58	45	4.6	2.2	90 000	160	562.5	large	C
30	ramesh	27	male	1385843	alcoholic	3 cms	no	+	encephalopathy	6	380	290	3.4	3.8	1.2	140	857.1	small	C
31	marudhamuthu	50	male	1387121	hepatitis B/C	5 cms	no	+		15.2	560	555	3	3.2	80 000	160	500	large	C
32	sheik abdulla	42	male	1387164	alcoholic	7 cms	+	+	encephalopathy	3.8	200	180	2.4	3.8	80 000	180	444.4	large	C
33	ayyadurai	55	male	1386657	hepatitis B	no	no	no		1	75	45	4.8	1.6	1.2 lakhs	100	1200	NO VARICES	A
34	vanita	27	female	1386781	hepatitis c	1 cm	+	+		5.2	180	220	3	3	1 lakh	140	714.2	small	C
35	albert	35	male	1387551	alcoholic	no	+	+		2.8	268	200	5	2	1.2 lakhs	120	1000	NO VARICES	B
36	velu	38	male	1387240	hepatitis B	2 cms	+	+	SBP	3	180	140	2	3.2	1.1 lakhs	140	785.7	small	C
37	parthiban	44	male	1387115	alcoholic	no	no	+		4.8	280	160	5.5	1.8	1.45	120	1208.3	NO VARICES	B
38	kumarselvam	35	male	1387543	alcoholic/hepat	1 cm	+	+		6	480	450	2.8	2.2	90 000	140	642.8	small	C
39	sashikala	31	female	1379998	hepatitis c	no	no	+		8.8	180	170	4.8	1.2	1.4 lakhs	130	1076.9	NO VARICES	B
40	ravichandran	57	male	1379419	alcoholic	2 cms	no	no		1.2	280	250	4.2	1.8	1.1 lakhs	140	785.7	small	A
41	annapan	45	male	1379766	alcoholic	4 cms	+	no		1.1	110	90	3	2.1	1.2 lakhs	150	800	small	B
42	ganapathi	32	male	1377092	alcoholic	2 cms	no	+		3	120	90	4.8	1	1.5 lakhs	140	1071.4	NO VARICES	A
43	velayutham	65	male	1381754	alcoholic	no	+	no		0.8	200	180	3	4	70 000	120	583.3	large	C
44	kaliyaperumal	50	male	1381778	alcoholic	2 cms	no	no		0.9	45	40	4.5	1.2	1.5 lakhs	138	1086.9	NO VARICES	A
45	sriram	27	male	1381743	alcoholic	4 cms	no	+		3	333	320	2	2	1 lakh	150	666.6	large	C
46	papathi	45	female	1394024	hepatitis B/C	5 cms	no	no		0.8	35	22	2	4	60 000	160	375	large	C
47	ramalingam	43	male	1391466	alcoholic/hepat	no	+	+		4.2	68	60	3	3.1	90 000	125	720	small	C
48	kalaiselvi	25	female	1379182	cryptogenic	1 cms	no	+		2.8	45	40	4.8	2.8	1.4 lakhs	140	1021.4	NO VARICES	A
49	Jayasudha	26	female	1381235	hepatitis c	5 cms	+	+		3.8	230	200	2	3.2	1.4 lakhs	160	875	large	C

S.No	NAME	AGE	SEX	IP NUMBER	ETIOLOGY	SPLENOMEGALY	ASCITES	ICTERUS	OTHERS	TOTAL BILIRUBIN	AST	ALT	SERUM ALBUMIN	PT-INR	PLATELET COUNT	SPLENOMEGALY(USG)	PSR	UGI SCOPY	CHILD'S SCORE
50	pugalselvi	25	female	1371182	cryptogenic	1	no	+		2.8	312	288	4	1.6	1.43 lakhs	138	1021.4	NO VARICES	A
51	jayendran	30	male		alco/hepc	3	+	+		3	423	400	3.5	2.4	1.2	140	873	large	C
52	rajeshwari	35	female	1376209	cryptogenic	no	no	no		1.2	39	36	4.5	1.6	1.4	130	1076.9	NO VARICES	A
53	kumar	40	male		alcoholic	2 cms	+	+		4.8	220	180	2	2	60 000	150	400	large	C
54	arumugam	53	male		alcoholic	1 cms	+	no		1.8	342	180	4	1.8	1.6 lakhs	130	1230.7	NO VARICES	A
55	marudhamuthu	45	male		alcoholic	3	+	no		1.2	200	180	3	2	1.2 lakhs	150	800	large	C
56	jayanthi	18	female		wilson's	1	+	+		3.2	112	78	3.5	1.8	1 l	135	740.7	small	B
57	sabapathy	32	male		alcoholic	2	+	+	encephalopathy	1.8	330	280	2	3.1	1 lakh	148	666.6	large	C
58	arunazaghi	20	female		cryptogenic	no	+	+		11.2	50	44	2.3	3.2	1lakh	110	909.09	small	C
59	subramaniyan	55	male		alcoholic/hep b	2	+	+		4.8	260	240	3	3.6	90 000	140	642.8	large	C
60	murugadass	58	male		alcoholic	3	no	+		2.6	130	75	3.5	2.1	1.2 lakhs	130	923	small	B

PROFORMA

NAME:

AGE/SEX

IP NUMBER

COMPLAINTS:

DURATION:

PRESENCE OF BLEEDING

MANIFESTATIONS:

H/0 ALCOHOL INTAKE:

H/0 BLOOD TRANSFUSIONS/

TATTOING/ IV DRUG ABUSE:

H/O DISEASE IN SIBLINGS

H/O OTHER MANIFESTATIONS

ETIOLOGY:

CLINICAL FEATURES:

GENERAL EXAMINATION:

PR: BP:

ICTERUS: OTHERS:

PER ABDOMEN:

SPLEENOMEGALY ASCITES

OTHERS:

INVESTIGATIONS-

TOTAL BILIRUBIN:

AST:

ALT:

SERUM ALBUMIN:

PT-INR:

PLATELET COUNT:

SPLEEN DIAMETER (USG):

CHILD-PUGH'S SCORE:

PLATELET COUNT/SPLEEN DIAMETER RATIO:

UGI SCOPY:

ABBREVIATIONS

OV- oesophageal varices

PSR- platelet count/spllen diameter ratio

PT-INR- prothrombin time-international normalized ratio

HCC- hepatocellular carcinoma

ALD- alcoholic liver disease

ADH- alcohol dehydrogenase

ALDH- aldehyde dehydrogenase

NAFLD- nonalcoholic fatty liver disease

NASH- nonalcoholic steatohepatitis

PBC- primary biliary cirrhosis

PSC- primary sclerosing cholangitis

AMA- antimitochondrial antibodies

pANCA- perinuclear antineutrophil cytoplasmic antibody

SBP- spontaneous bacterial peritonitis

LFT- liver function test

ALT- alanine aminotransferase

AST-aspartate aminotransferase

PT- prothrombin time

MELD- model for end stage liver disease

CT- computerized tomography

HVPG- hepatic vein pressure gradient

UGI SCOPY- upper gastro-intestinal scopy

CE- capsule endoscopy

EUS- endoscopic ultrasound

USG- ultrasonography

TE- transient elastography

MRI- magnetic resonance imaging

EST- endoscopic sclerotherapy

EVL- endoscopic variceal ligation

TIPS- transjugular intrahepatic portosystemic shunts

SD- standard deviation

Figure : 1

Endoscopic image of OV at the gastroesophageal junction.

Figure 2 :
Small varices on UGI SCOPY.

Figure 3 :
Large varices on UGI SCOPY

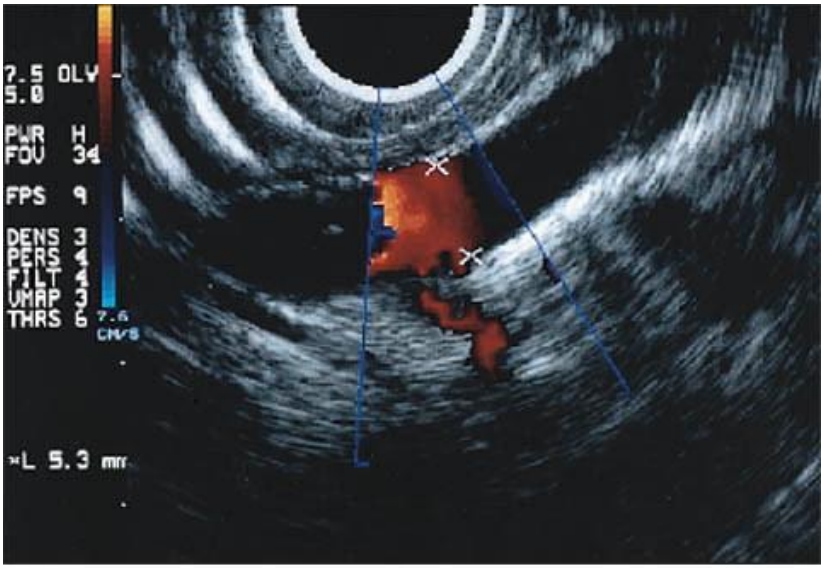


Figure 4 : Azygos vein demonstrated by Doppler EUS. Red indicates cephalad blood flow

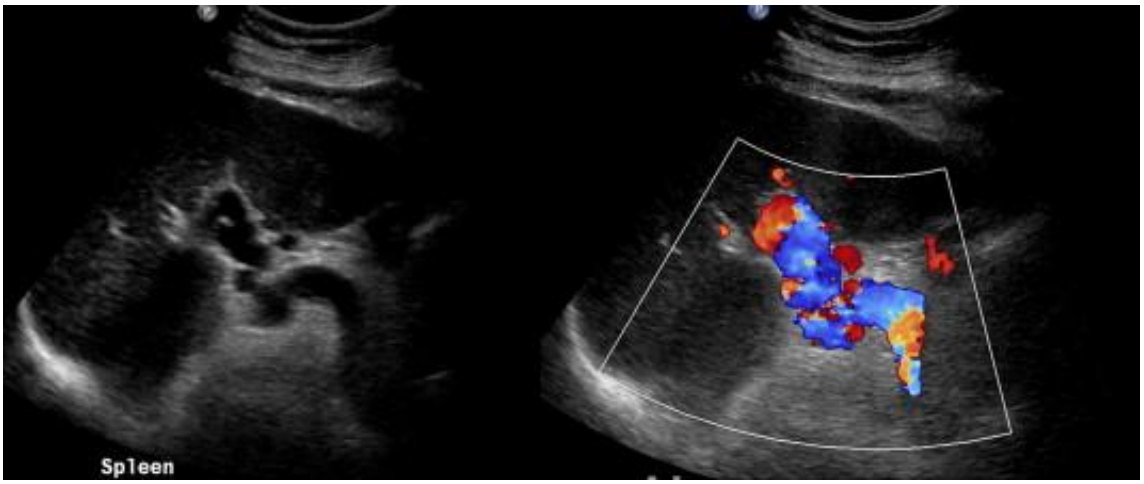


Figure 5 : Grey-scale imaging showing an enlarged spleen, dilated splenic vein and splenorenal varices. Doppler imaging of the same patient confirms the presence of varices.

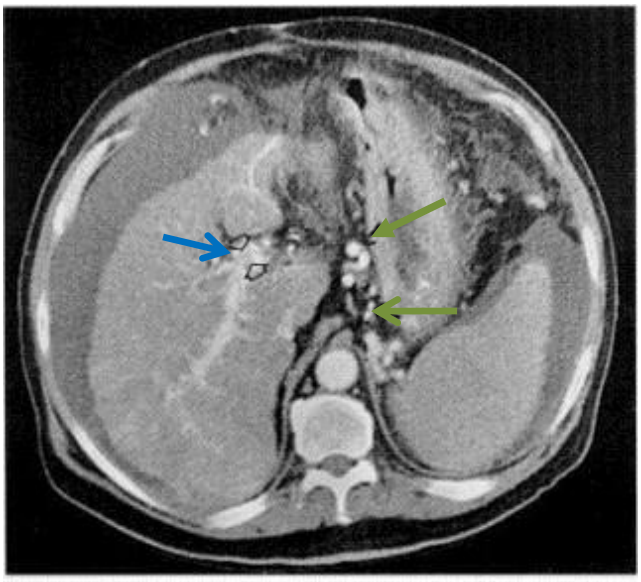


Fig. 6 Enhanced CT scan shows a lobulated contour of the liver, splenomegaly, portosystemic collaterals (red arrows), and ascites. There are enlarged hepatic arterial collateral vessels and thrombus within the portal vein (blue arrows)

Fig. 7 MRI of the portal venous system demonstrates extensive esophageal varices (arrows) in conjunction with splenic and gastric varices

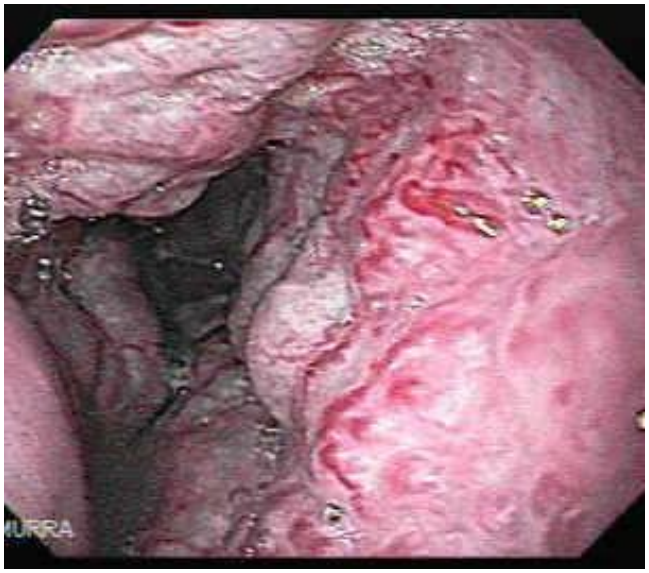


Fig. 8 : Endoscopic image showing large varices with red wale markings.

Fig 9 : Endoscopic image showing varices with cherry red spots.

Thanjavur Medical College

THANJAVUR, TAMILNADU, INDIA-613004

(Affiliated to the T.N Dr.MGR Medical University, Chennai)

ETHICAL COMMITTEE

CERTIFICATE

Name of the Candidate	: Dr.ASHWINI KAMATH
Course	: M.D (GENERAL MEDICINE)
Period of Study	: OCTOBER 2011- OCTOBER 2012
College	: THANJAVUR MEDICAL COLLEGE
Dissertation Topic	: NON INVASIVE PREDICTOR OF OESOPHAGEAL VARICES IN CIRRHOSIS - PLATELET COUNT / SPLEEN DIAMETER RATIO

The Ethical Committee, Thanjavur Medical College has decided to inform that your Dissertation Topic is accepted and you are permitted to proceed with the above study.

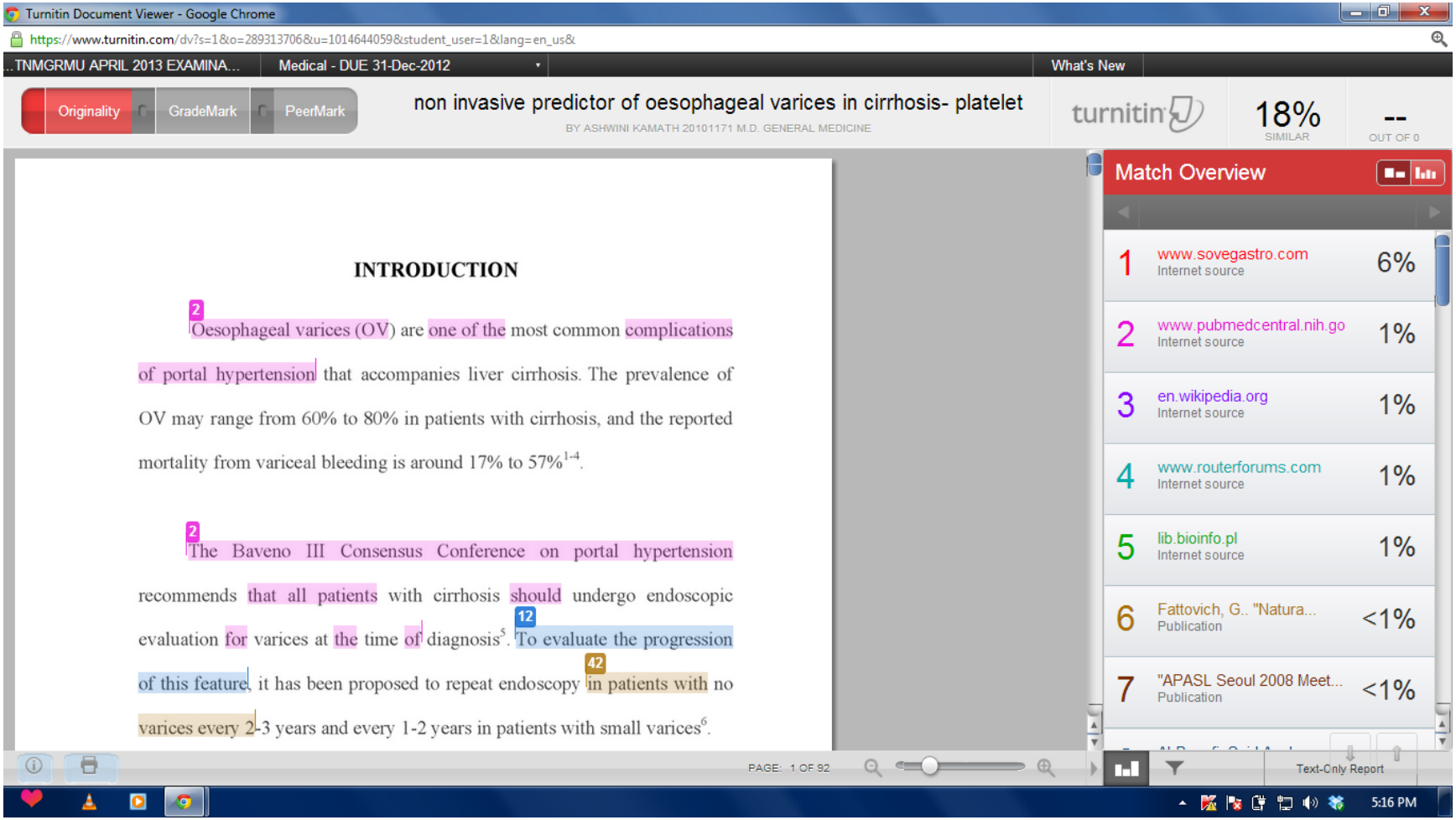
Thanjavur

Date :

THANJAVUR MEDICAL COLLEGE THANJAVUR-4.

Secretary

Ethical Committee


Turnitin Document Viewer - Google Chrome
https://www.turnitin.com/dv?s=1&o=289313706&u=1014644059&student_user=1&lang=en_us&
...TNMGRMU APRIL 2013 EXAMINA...
Medical - DUE 31-Dec-2012
What's New
Originality
GradeMark
PeerMark
non invasive predictor of oesophageal varices in cirrhosis- platelet
BY ASHWINI KAMATH 20101171 M.D. GENERAL MEDICINE
turnitin
18%
SIMILAR
--
OUT OF 0
INTRODUCTION
Oesophageal varices (OV) are one of the most common complications of portal hypertension that accompanies liver cirrhosis. The prevalence of OV may range from 60% to 80% in patients with cirrhosis, and the reported mortality from variceal bleeding is around 17% to 57%[1-4].
The Baveno III Consensus Conference on portal hypertension recommends that all patients with cirrhosis should undergo endoscopic evaluation for varices at the time of diagnosis[5]. To evaluate the progression of this feature, it has been proposed to repeat endoscopy in patients with no varices every 2-3 years and every 1-2 years in patients with small varices[6].
PAGE: 1 OF 92
Match Overview
1 www.sovegastro.com Internet source 6%
2 www.pubmedcentral.nih.go Internet source 1%
3 en.wikipedia.org Internet source 1%
4 www.routerforums.com Internet source 1%
5 lib.bioinfo.pl Internet source 1%
6 Fattovich, G.. "Natura... Publication <1%
7 "APASL Seoul 2008 Meet... Publication <1%
Text-Only Report
5:16 PM

turnitin

Your digital receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

Paper ID	289313706
Paper title	non invasive predictor of oesophageal varices in cirrhosis- platelet count/spleen diameter ratio
Assignment title	Medical
Author	Ashwini Kamath 20101171 M.D. General Medicine
E-mail	kamath08@gmail.com
Submission time	19-Dec-2012 12:52AM
Total words	11775

First 100 words of your submission

INTRODUCTION Oesophageal varices (OV) are one of the most common complications of portal hypertension that accompanies liver cirrhosis. The prevalence of OV may range from 60% to 80% in patients with cirrhosis, and the reported mortality from variceal bleeding is around 17% to 57% 1-4 . The Baveno III Consensus Conference on portal hypertension recommends that all patients with cirrhosis should undergo endoscopic evaluation for varices at the time of diagnosis 5 . To evaluate the progression of this feature, it has been proposed to repeat endoscopy in patients with no varices every 2-3 years and every 1-2 years in patients with small varices 6 . In a developing nation like ours where there...